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Data indicate that for sinusoidal acceleration of 1, 2, and 3 cycles per minute at amplitudes of 0 to $+2g_z$ and $+1$ to $+2g_z$, the cardiovascular system of chronically instrumented dogs was capable of following with peak to peak responses equal to those obtained for sustained tests with mean responses correlatable with the mean g level of the test. The usefulness of the awake, chronically instrumented canine as a surrogate for man under conditions of orthostatic loading along the spinal axis was studied and the cardiovascular

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20. responses were found to be similar. It was further suggested the canine might also be used as a surrogate for man in non-extreme states of cardiovascular deconditioning. Other data suggests that in these subjects the combined stress of $+g_z$ orthostasis and $g_z$ vibration produces a more sensitive cardiovascular system capable of responding with larger changes in mean aortic flow than those seen with $g_z$ vibration alone.

RESPONSE OF THE CARDIOVASCULAR
SYSTEM TO VIBRATION AND COMBINED STRESSES

Progress Report
1974-1975
Air Force Office of Scientific Research
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University of Kentucky

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August 31, 1975

## ACKNOWLEDGEMENTS

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# I. PROGRAM SUMMARY 1974-1975

The goal of this program is the understanding of cardiovascular responses to force-field loading of the total physiological system. Force fields may be due to earth gravity or forces produced by whole body acceleration. Acceleration forces may be either static, slowly varying, or extremely fast relative to the cardiovascular system's capability to respond. Understanding of these responses implies qualitative and quantitative evaluation of the cardiovascular changes produced by the acceleration loading and knowledge about the mechanism responsible for eliciting these adjustments. Our efforts in the past were limited to understanding the cardiovascular responses to high frequency whole body acceleration (>1 Hz) but more recently have been extended to the domain between sustained and time-varying acceleration of less than 1 Hz.

The effects of acceleration stress may be evident at the time of exposure or may produce delayed reactions through chronic alterations. Maximum effectiveness in meeting military objectives requires understanding of the physiological adjustments to the full range of acceleration stresses and is a problem unique to military medicine in general and to aero-space medicine in particular for those stresses encountered in flight operations. Our current efforts devoted to this understanding are summarized below and presented in more detail in the body of this report.

## A. Cardiovascular Responses of Canines to Sustained and Low Frequency Sinusoidal Acceleration (0 up to 0.05 Hz)

The purpose of this study was to quantify mean cardiovascular changes in chronically instrumented canines as a function of sustained and slowly-varying sinusoidal acceleration. All of the cardiovascular responses measured in these studies were qualitatively and quantitatively similar for the 0 to $+1$ $g_z$ tilt and 0 to $+1$ $g_z$ sustained centrifugation test. Stroke volume, mean aortic flow, systolic, diastolic and mean aortic pressures, systolic right ventricular pressure and

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left ventricular dP/dt decreased from control. Heart rate and peripheral vascular resistance increased. All variables which decreased their values from control for the +1 $g_z$ sustained test, decreased their values even further for the +2 $g_z$ tests. However, heart rate and peripheral vascular resistance which increased from control for the 0 to +1 $g_z$ test showed no further significant increase for the 0 to +2 $g_z$ tests.

When the animals were exposed to a +2 $g_z$ stress after a +1 $g_z$ control period (produced either by centrifugation or orthostasis) the responses were less consistent. Prolonged +1 $g_z$ orthostasis was thought to be responsible for the decreased responses to +2 $g_z$ loading observed in the aortic pressure measurements.

When acceleration stress was varied sinusoidally at approximately 1, 2, and 3 cycles per minute (at the same peak to peak acceleration amplitude as those produced during the sustained tests), responses meaned over the test period were found to correlate with the mean g level during the test period only, and not with the frequency of oscillation. Those variables which showed a lack of correlation were heart rate and peripheral vascular resistance. The rates of decrease in mean aortic flow, and aortic systolic and diastolic pressures with increasing mean g levels were greater when the animal was in the horizontal position than the vertical position with respect to earth gravity. Stroke volume responses which also decreased with increasing mean g were independent, however, of whether the animal was horizontal or vertical. In fact, stroke volume was the only cardiovascular variable whose changes were consistent from test to test and dog to dog, and was the least affected by the way in which the acceleration stress was produced, i.e. tilt or centrifugation.

Taken collectively, these results indicate that for sinusoidal accelerations of 1, 2, and 3 cycles per minute at amplitudes of 0 to +2 $g_z$ and +1 to +2 $g_z$, the cardiovascular system was capable of following with peak to peak responses

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equal to those obtained for sustained tests and with mean responses correlatable with the mean g level of the test.

B. Comparison of the Orthostatic (+1 $g_z$) Tolerance of Awake Canines to that of Normal and Cardiovascularly Deconditioned Humans

The usefulness of the awake, chronically instrumented canine as a surrogate for man under conditions of orthostatic loading along the spinal axis was studied. The cardiovascular response of these canines was found to be much the same as that of normal humans, however there was enough difference to indicate that the canine might also be studied as a surrogate for man in a non-extreme state of cardiovascular deconditioning.

In this study, for all tests, heart rate increased and stroke volume decreased which when combined showed a decrease in cardiac output in each case. Aortic systolic and diastolic pressures decreased in all tests but one, and in it there was no change. Coronary blood flow showed a characteristic time-variation where the immediate response to tilt was increased coronary flow followed by a decrement in flow over the remaining test period, with a net result of no appreciable change from control when averaged over the five minute test period. Maximum dP/dt consistently showed an initial sharp increase followed immediately by a decrease below normal that lasted throughout the test session. Right ventricular systolic pressure decreased, while left and right ventricular diastolic pressures showed inconsistent responses. The magnitude of the T segment of the ECG over the five minute test period was often seen to change.

A response common to normal man, cardiovascularly deconditioned man, anesthetized canines and awake canines was a 40% decrease in stroke volume with orthostatic stress; differences appear in the subjects' response to this common decrease. The noninvasive orthostatic index of Burkhart and Kirchoff was calculated for normal and cardiovascuarly deconditioned humans and for the awake

canines and does appear to be an index of the degree of cardiovascular tolerance
to orthostatic loading.

C. Comparison of Cardiovascular Responses in Canines Restrained Vertically
and Horizontally to $g_z$ Sinusoidal Vibration (2-20 Hz)

To delineate the influence of $+g_z$ orthostasis on cardiovascular responses
to $g_z$ sinusoidal vibration, studies were performed on chronically instrumented
canines restrained horizontally with respect to earth gravity and exposed to the
same protocol as those restrained vertically in previous studies conducted on
the vibration table. The principal finding was the marked decrease in mean aortic
flow response to whole body vibration for the canines restrained vertically as
compared to those in the horizontal position. The vertical subjects were shown
to markedly increase mean aortic flow with increasing transmitted force, while
the horizontal subjects showed a minor increase. Increases in mean aortic flow
for the animals restrained horizontally were produced principally by increases
in heart rate in contrast to the vertical case in which some increased their
mean aortic flow mainly by stroke volume changes, others by heart rate changes,
and others by a combination of both. It was also observed that control stroke
volume for the vertical subjects was approximately 40% less than that of the
horizontal subjects. These decreased values are thought to be a result of blood
pooling in the periphery due to the $+1$ $g_z$ orthostatic loading. The combined
stress of $+g_z$ orthostasis and $g_z$ vibration appears to produce a more sensitive
cardiovascular system capable of responding with larger changes in mean aortic
flow than those seen with $o_z$ vibration alone.

D. Acceleration Transmissibility of Internal Organs in Canines Exposed to Whole
Body Vibration (2-12 Hz)

Studies were conducted to measure the $g_z$ acceleration transmissibility of
individual organ systems. Data from these studies will aid in understanding
the mechanisms by which vibration-induced cardiovascular pressure/flow changes

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are produced. Accelerometers were acutely implanted on the heart, diaphragm, and sternum. The animals were exposed (30 seconds) to sinusoidal vibration at discreet frequencies in the range of 2-20 Hz and acceleration amplitudes of 0.75, 1.0, and 1.25 $g_z$, for both the animals restrained horizontally and vertically with respect to earth gravity. Normalizing absolute organ acceleration responses by measured table acceleration yielded a closely fitting family of transmissibility modulus (TM) curves for the various g levels employed. It was found that the TM of the diaphragm, heart and sternum tended to be higher for the horizontal cases than for the vertical cases: as much as 90% higher for the peak response of the heart and diaphragm. The primary resonant frequency for the three anatomical sites was higher for the vertical vibration mode occurring at a frequency of 4-6 Hz compared to the 3-4 Hz for the horizontal case. The response of all three anatomical sites beyond 10 Hz was essentially damped. Transmissibility phase angle (TPA) was similar for both the horizontal and vertical vibration modes. Heart and diaphragm appeared to "track" together through the entire frequency range. At all three anatomical sites TPA increased from 0 at low frequencies (2 Hz) through 90° near the resonant frequency.

In one animal intra-thoracic pressure was measured and found to correlate directly with diaphragm acceleration, i.e. tending to be greater in amplitude for greater diaphragm acceleration. The fluctuations in intra-thoracic pressure due to the diaphragm "pumping" caused by vibration are of sufficient amplitude to suggest a possibility of vibration-induced alterations in the dynamics of venous return and right atrial filling.

E. Instrumentation and Data Acquisition Development: An Improved Technique For Determination of Left Ventricular Max dP/dt and (Max dP/dt)/P

The addition of the Raytheon 704 data acquisition and analysis system has resulted in improvements not only in the ability to accurately measure the data, but also has proved to be a more accurate technique for determining both the

magnitude and time of occurrenace of maximum left ventricular dP/dt. The conventional "op-amp differentiator circuit/hard copy recorder" system normally used was found to nave two drawbacks: one is the phase lag introduced by the differentiator and the other is the absolute value of maximum dP/dt which can be incorrectly interpreted from conventional calibration procedures. The significance of the improved computer technique lies not only in the increased value of maximum dP/dt observed, but more importantly in the accuracy of the determination of the place where maximum dP/dt occurs with respect to the left ventricular pressure trace. At least two of the indices of contractility (maximum dP/dt)/P and dP/dt at 40 mn Hg pressure require accurate measurements of the pressure at which the derivative occurs.

F. Publications Resulting From This Research Program

Bhattacharya, A., Knapp, C.F., McCutcheon, E.P., and Edwards, R.G.: "A Study of Meaningful Vibration Parameters for Assessing the Response of the Cardiovascular System", Proceedings of the 1975 Aerospace Medical Association Meeting, San Francisco, California, April 28, 1975.

Knapp, C.F. and Marquis, J.A.: "Acceleration Transmissibility of Internal Body Organs in Canines Exposed to Whole Body Vibration", Proceedings of the 1975 Aerospace Medical Association Meeting, San Francisco, California, April 28, 1975.

Bhattacharya, A., Knapp, C.F., McCutcheon, E.P., and Evans, J.M.: "Comparison of Cardiac Responses to Nonsynchronous and Heart Synchronous Whole Body Vibration", Proceedings of the 28th Annual ACEMB, New Orleans, Louisana, September, 1975.

Edwards, R.G., Lafferty, J.F., and Knapp, C.F.: "Experimental and Analytical Determinations of the Mechanical Impedance Response of Animals to Vertical Vibration", Accepted for Publication, Journal of Biomechanics.

McCutcheon, E.P., Evans, J.M., and Wibel, F.: "A Fabric Pouch For Multiple Chronically Implanted Transducer and Catheter Terminations", Accepted for Publication, Journal of Applied Physiology.

Bhattacharya, A.: "Modification of Cardiac Function by Heart Synchronous Whole Body Vibration Applied to Awake Chronically Instrumented Canines", Ph.D. Dissertation, University of Kentucky, 1975 (Abstract in Appendix A).

Bhattacharya, A., Knapp, C.F., McCutcheon, E.P., and Edwards, R.G.: "Parameters for Assessing the Response of the Cardiovascular System of Awake Chronically Instrumented Canines Exposed to Whole Body Vibration", Accepted for Publication, Journal of Applied Physiology.

Evans, J.M., Knapp, C.F., and Lafferty, J.F.: "Comparison of the Orthostatic ($+1 g_z$) Tolerance of Awake Canines to that of Normal and Cardiovascularly Deconditioned Humans", In Progress.

II.  PROGRESS REPORT 1974-75

A. Cardiovascular Responses of Canines to Sustained and Low Frequency Sinusoidal
   Acceleration (0 up to 0.05 Hz)

## INTRODUCTION

Recent advances in sophisticated high performance aircraft have produced a need for understanding cardiovascular responses to high amplitude, slowly-varying acceleration. A critical lack of data presently exists in the area between sustained acceleration and time-varying acceleration at frequencies of 1.5 Hz and less. In order to fill the need, quantification of cardiovascular responses of canines to time-varying acceleration of less than 1.5 Hz was initiated. A 50 foot diameter centrifuge was programmed to vary the rotation rate in order to produce sinusoidally-varying acceleration forces at different frequencies. Also, tilt table and sustained acceleration tests were conducted as control experiments in order to establish a basis for comparison with data from the sinusoidally-varying acceleration experiments.

## METHODS

Canines were chronically instrumented for continuous measurements of ascending aortic flow (Zepeda), left ventricular pressure (Konigsberg), circumflex coronary flow (Biotronics; plus occlusive zero). On the day of the experiment the subject was tranquilized with INNOVAR-VET[t] at 1 cc/10 kg body weight IV and, under local anesthesia, both a femoral vein and an artery were cannulated for passage of manometer-tipped catheters (Millar Instruments) into the left and right ventricles. After calibration of the implanted left ventricular gauge, via the acutely placed Millar gauge, the Millar gauge was pulled back into the aorta just outside the valve and tied in for the remainder of the study. The measured variables included mean aortic pressure, heart rate, systolic aortic pressure, diastolic aortic pressure, right ventricular pressure, stroke volume, cardiac output, coronary flow, and left ventricular pressure, power density and dP/dt.

Next, the animal was restrained in the supine position and sufficient time was allowed for the variables to stabilize before initiating the experiments. Each experiment consisted of the following tests:

1) Horizontal to vertical tilt, 0 to +1 $g_z$

The animal was tilted to the vertical position and all variables monitored for a five minute test period. Five minutes was thought to be sufficient because the cardiovascular responses appeared to stabilize within this time. The test period was also chosen to compare results with some of the previous studies, especially those using humans, in which a five minute test period was employed. Following tilt, the animal was returned to the horizontal position for a ten minute re- covery period. Each animal was tested two or three times in the same day.

2) Sustained acceleration exposures of 0 to +1 $g_z$, and 0 to +2 $g_z$

The animal restraint chair was horizontal with respect to earth gravity (Figure 1). The test period for each was approximately five minutes with control periods between the tests of approximately four minutes.

3) Sustained acceleration of +1 to +2 $g_z$

Two methods were employed:

a) The animal restraint chair was horizontal and the five minute +1 $g_z$ control loading was produced by centrifuge rotation prior to the +2 $g_z$ sustained test (Figure 1).

b) The animal restraint chair was vertical during the control period and aligned itself with the resultant acceleration vector during the +2 $g_z$ test (Figure 2).

Fig. 1. Modification of existing centrifuge to accommodate a horizontally-restrained canine for exposure to $g_z$ sinusoidal acceleration via changes in RPM.
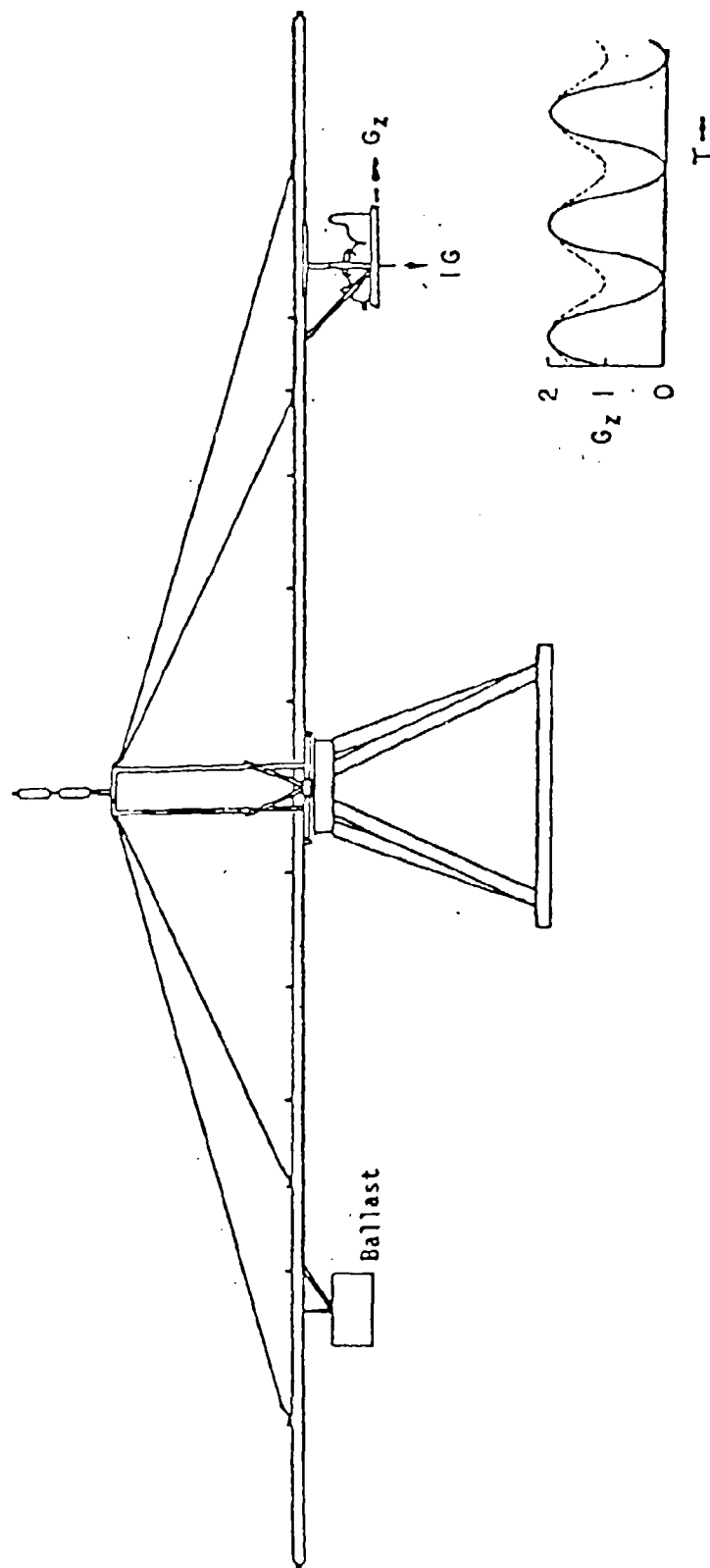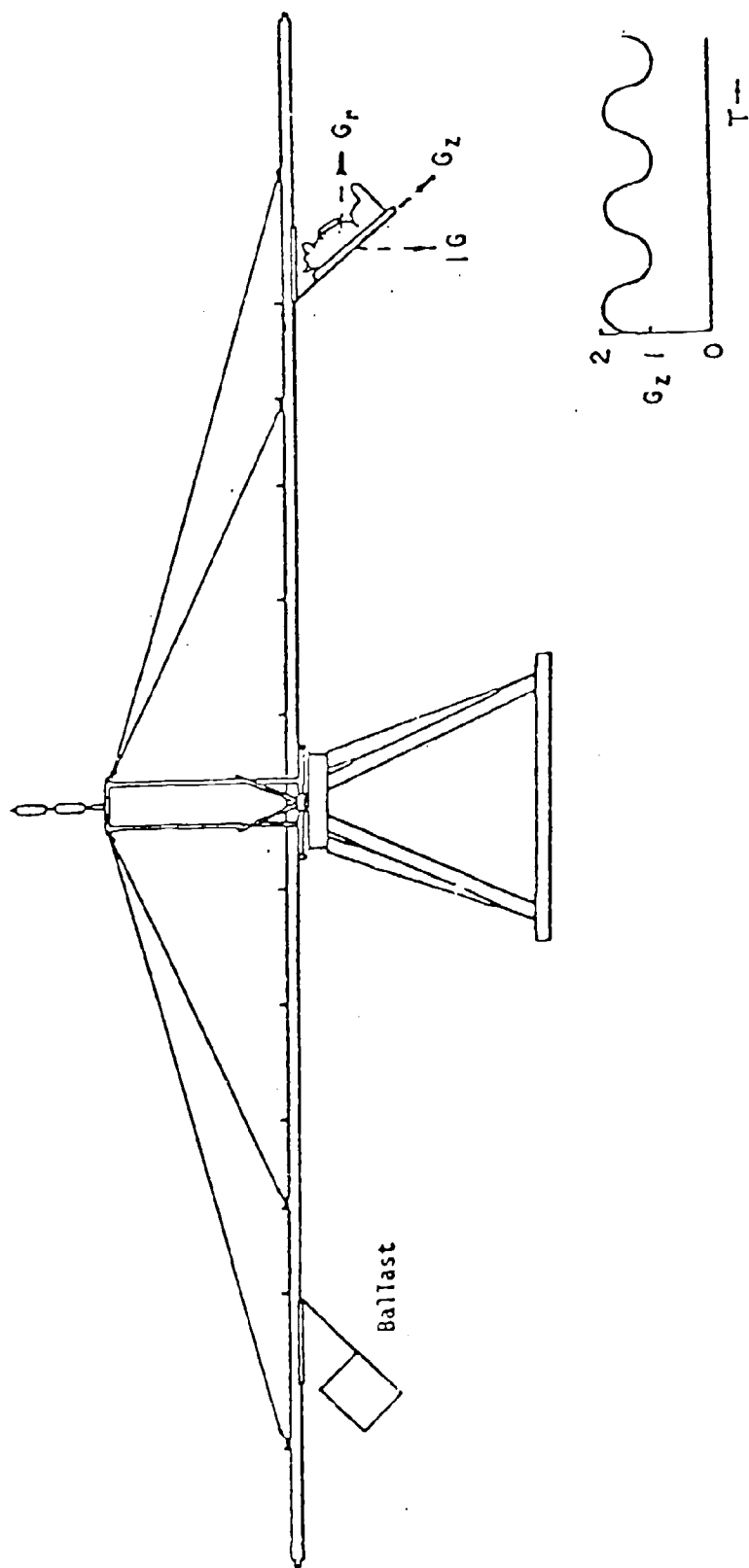
Fig. 2. Modification of existing centrifuge to accommodate a vertically-restrained canine for exposure to $g_z$ sinusoidal acceleration via changes in RPM.

4) <u>Sinusoidal acceleration of 0 to +2 $g_z$ and +1 to +2 $g_z$</u>

Frequencies of 0.0017, 0.032, and 0.050 Hz (~1, 2, and 3 cycles per minute, CPM) were chosen with acceleration amplitudes of

a) 0 to +2 $g_z$ and +1 to +2 $g_z$ (Figure 1), and

b) +1 to +2 $g_z$ as illustrated in Figure 2.

The exposure time of the sinusoidally-varying acceleration was adjusted, depending upon the frequency, to get a sufficient number of cycles for analysis. The average time of exposure was five minutes.

## RESULTS

Fourteen different protocols (133 tests) were performed on nine days on six different animals. Results are reported from 87 tests on six days using four different animals. Data from three days were rejected since there was evidenced that those animals had impaired cardiovascular systems and should be considered separately. Two of the three had no control left circumflex coronary flow, very low stroke volume (14 ml) yielding low cardiac output (1.6 L/min) with an elevated systolic right ventricular pressure (>50 mm Hg). The other animal also had low stroke volume (11 ml) elevated heart rate (125 b/min) low cardiac output (1.4 L/min), low aortic systolic (82 mm Hg), and diastolic (45 mm Hg) pressures with almost nonexistant systolic right ventricular pressure (5 mm Hg) and was found to be unable to tolerate +2 $g_z$ in a later test. The response data of the first two was discarded based on the above and on pathological evidence of myocardial infarction occurring downstream of the implanted left circumflex coronary artery flow probe and occluder at some time (<14 days) prior to the test. The inability of the third animal to maintain heart rate, flow or pressure at +2 $g_z$ made the +1 $g_z$ response questionable, particularly when viewed in light of his extremely low control (horizontal) values also. The other six dogs (87 tests) were judged to be normal both in control values and in their ability to respond to stress.

## Tilt Tests

The details of the tilt table study and a comparison of the results with those for humans is presented in the section entitled "Comparison of the Orthostatic ($+1$ $g_z$) Tolerance of Awake Canines to that of Normal and Cardiovascularly Deconditioned Humans". A summary of the results which will be used for comparison purposes in this section follows.

The results of the tilt studies are shown in Figure 3. The data for "control" and "test" were each averaged over the five minute period. Each bar in Figure 3 represents the five minute averages meaned over all animals with the plus or minus standard error of the mean (SEM = $\frac{S.D.}{\sqrt{n}}$) shown. In all tests except one, both systolic and diastolic aortic pressures decreased, and in that case there was no change. In all tests, heart rate increased and stroke volume decreased which, when combined, showed a decrease in cardiac output in each case. Coronary flow showed a characteristic time variation; where the immediate response to tilt was increased coronary flow, followed by a decrement in flow over the remaining test period, with a net result of no appreciable change from control when averaged over the five minute test period. Maximum dp/dt consistently showed an initial short increase followed immediately by a decrease below normal that lasted throughout the test session for an average decrease of $-12.6 \pm 2.0\%$. Power density, the integrated plot of dLVP/dt vs LVP over each heart cycle showed approximately a 15% decrease over the test period. Left ventricular diastolic pressure decreased in 9 cases ($-2.0 \pm .5$ mm Hg) and increased in the other four ($+3.7 \pm 1.9$ mm Hg) with tilt for an average change of $-.2 \pm 1.0$ mm Hg. ECG (sternal lead) showed initial changes with tilt that were attributed to the relative shift of electrode positions with respect to the heart, but also over the five minute test sessions the magnitude of the segment was often seen to change with time. Systolic right ventricular pressures
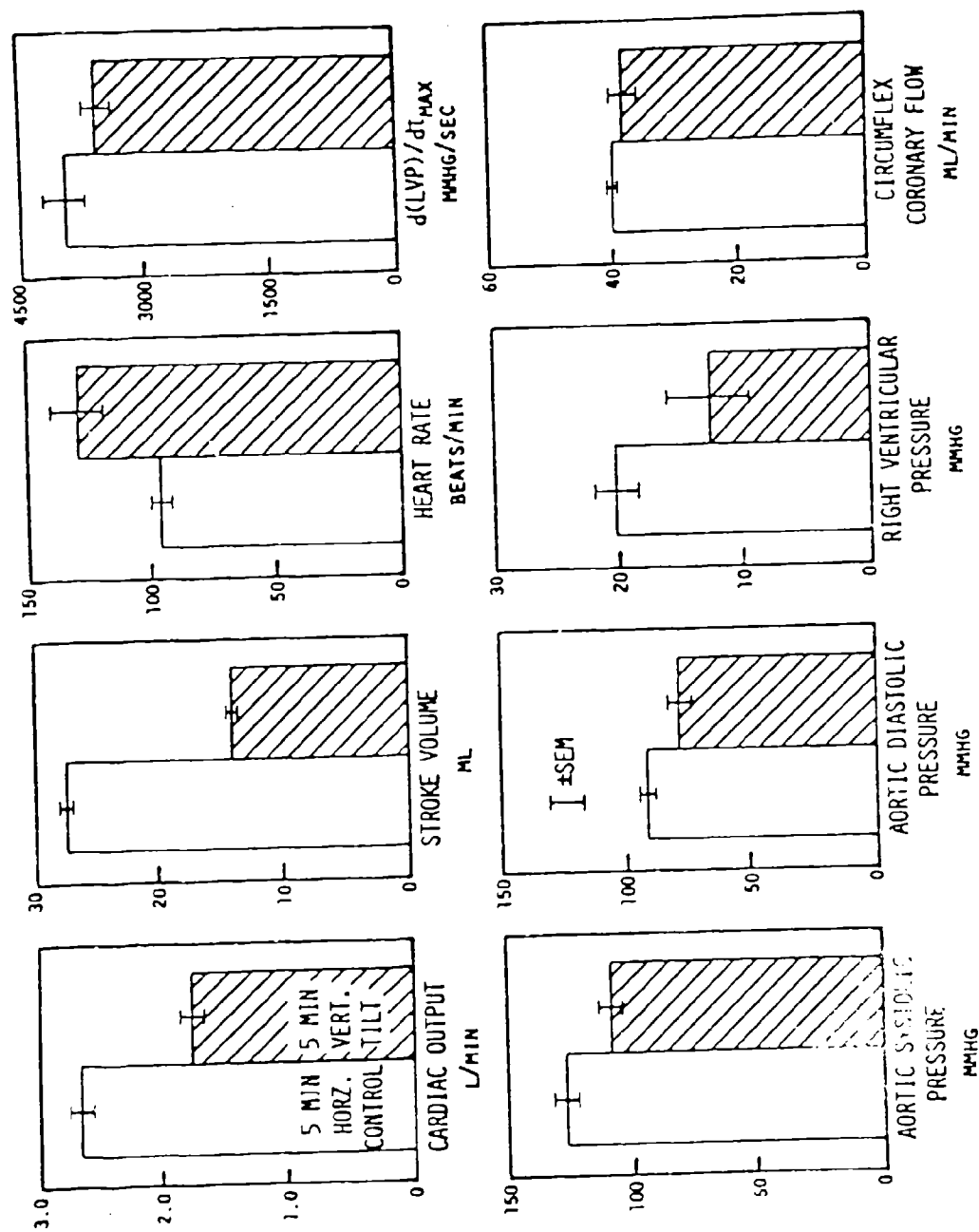
Fig. 3. Five minute averages of control (horizontal) and test (vertical) values ± S.E.M. for 14 tests on six awake, chronically instrumented canines.

decreased in 8 of 10 cases, (-40 ± 18%) while diastolic right ventricular pressure increased in four cases, (1.4 ± .5 mm Hg) and decreased in six (-2.4 ± 1.0 mm Hg) for an average change of -.9 ± .8 mm Hg.

## Sustained Acceleration Produced by Centrifugation

Typical responses to 0 to +2 $g_z$ acceleration stress are shown in Figure 4. The animal chosen was the one for which inferior vena cava flow was substituted for coronary flow and pulmonary artery pressure for right ventricular pressure. Obvious responses for this animal were tachycardia (heart rate increase of 83%), reduced aortic systolic and diastolic pressures (a mean of -41% and -47% respectively), decreased pulmonary artery systolic and diastolic pressures (-24 mm Hg and -5 mm Hg respectively), decreased mean aortic flow and stroke volume (mean of -50% and -72% respectively), decreased return of blood from the lower body segment as shown by decreased inferior vena cava flow (-54%), decreased maximum dP/dt (-24%) and a change over the five minute test period in the ST segment of the ECG.

The transient response of each variable to the rate of onset of the sustained acceleration is also of considerable interest, but is beyond the scope of this report. However, the analysis of such responses will be included in a subsequent document. The results reported here will be those concerned only with mean changes throughout the five minute test period.

In Figure 5, stroke volume, heart rate, mean aortic flow, systolic, diastolic and mean aortic pressure, right ventricular systolic pressure, left ventricular dP/dt, and peripheral vascular resistance are presented for the five procedures in which sustained +1 and +2 $g_z$ loadings were achieved. Each bar in Figure 5 represents the five minute averages meaned over the six animals. The ± S.E.M. is also shown. The first column consists of control and test values of 0 to +1 $g_z$ produced by tilting the animal vertical from the horizontal position. The
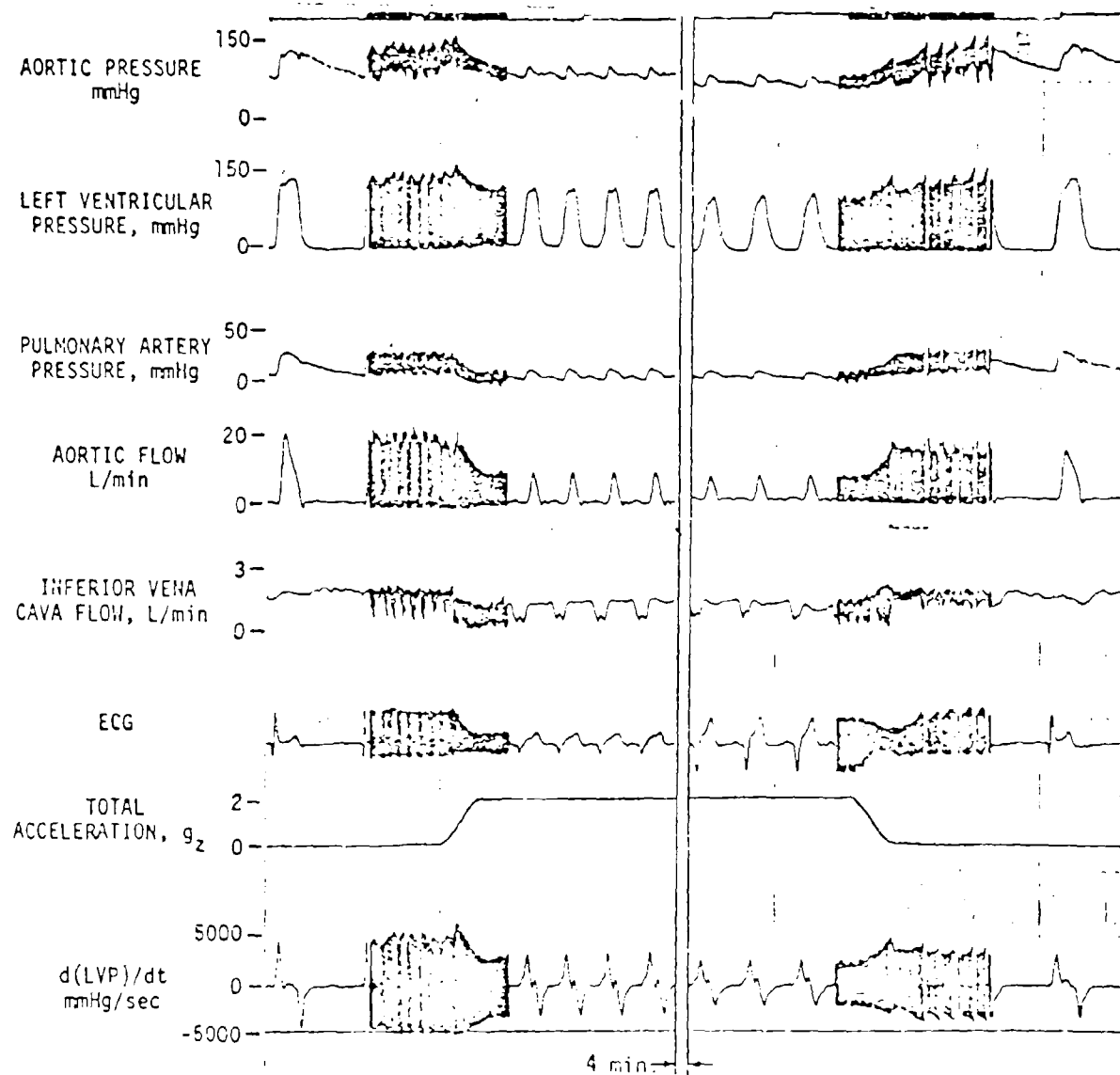
Fig. 4. Typical cardiovascular responses to 0 to +2 $g_z$ sustained acceleration (5 min exposure).
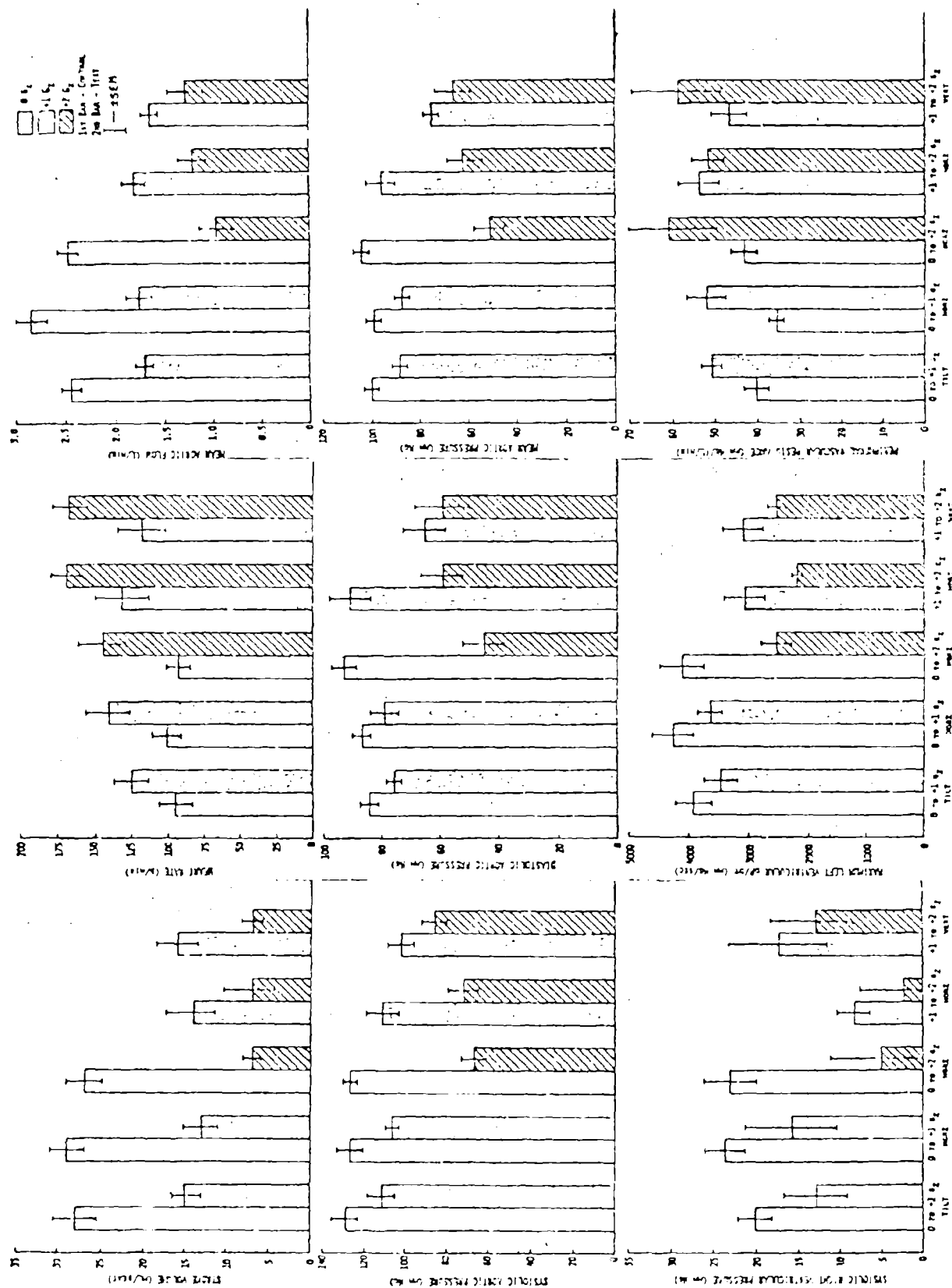
Fig. 5. Mean cardiovascular responses as a function of sustained +$g_z$ loadings.

results in the second column are for a +1 $g_z$ sustained test produced by centrifuge rotation with the animal fixed horizontal with respect to earth gravity (Figure 1). Data presented in column 3 is for the same situation as column 2 except that a +2 $g_z$ sustained test was conducted. In column 4, the animal is restrained in the same configuration as columns 2 and 3, but the +1 $g_z$ control was produced by centrifuge rotation and the test acceleration was +2 $g_z$. Unfortunately, only three animals were run on this particular protocol (note the large S.E.M.), but the data is included here for completeness. In column 5, the control and test g levels were the same as column 4 but the +1 $g_z$ control was obtained by allowing the animal restraint system to hang vertical before the test and align itself with the relative acceleration vector for the +2 $g_z$ loading (Figure 2).

All of the above variables except heart rate and peripheral vascular resistance decreased from control for the +1 and +2 $g_z$ stress. Heart rate and peripheral vascular resistance generally increased. A comparison of the results indicates that the cardiovascular responses are the same for +1 $g_z$ sustained loading whether produced by tilt or centrifugation (columns 1 and 2 respectively). Responses to +2 $g_z$ sustained acceleration were greater than those for the +1 $g_z$ acceleration. Generally, the +2 $g_z$ responses (test values of columns 3, 4, and 5) were within the same limits regardless of the control conditions (control values of columns 3, 4, and 5). It was also observed that the control results for column 5 (animal vertical) and the test results for column 1 (animal vertical from tilt test) were generally within the same limits. A notable exception was diastolic and, therefore, mean aortic pressure. Likewise, the +1 g control for column 4 (produced by centrifugation) and the +1 g test results of column 2 (produced by centrifugation) were also within the same limits except for right ventricular systolic pressure. The stroke volume response during the +1 $g_z$ and +2 $g_z$

sustained acceleration tests were independent of the control conditions and the technique used to produce the loading stress, i.e. tilt or centrifugation. The responses were very consistent both within subjects and across subjects.

It must be noted however, that the control values for column 5 represent a five minute sample taken from the end of an approximately 30 minute time period (due to centrifuge start-up procedures) during which the animal was in a vertical position. A comparison of these values with the $+1\ g_z$ test values of columns 1 and 2 shows definitely diminished diastolic and mean aortic pressures and slightly diminished heart rate, peripheral vascular resistance and dP/dt, probably as a result of the length of time spent at $+1\ g_z$. The $+2\ g_z$ test values (column 5) of the above mentioned variables following the prolonged control period were generally elevated over those of columns 3 and 4 perhaps due to an adaptation to the lengthy $1\ g_z$ control. The unclear responses of column 4 such as in the peripheral vascular resistance values both for control and test must be considered in light of the limited number of tests done (3 dogs).

Several variables were measured for which there will be no graphical results presented: power density, the integrated plot of dP/dt vs LVP over each heart cycle showed an ~15% decrease with tilt, and an ~23% decrease with 0 to $+1\ g_z$ centrifugation and a 66% decrease with 0 to $+2\ g_z$ centrifugation. Left circumflex coronary flow increased slightly in most animals for 0 to $+1\ g_z$ tests increased in two and decreased in two animals during the 0 to $+2\ g_z$ test, and increased in two and decreased in two during the $+1$ to $+2\ g_z$ vertical test. A characteristic of coronary flow under any $+\ g_z$ stress was an initial increased flow with the onset of the g stress followed by a gradual tapering off over the five minute test period. Neither left ventricular diastolic pressure nor right ventricular diastolic pressure showed a predictable response with $+g_z$ stress. More animals decreased diastolic pressures than increased them, but the variability

was extensive and several animals showed both increases and decreases in the same day to the same g loading.

## Slowly-Varying, Sinusoidal Acceleration Produced by Centrifugation

Typical cardiovascular responses to sinusoidal oscillations from 0 to +2 $g_z$ at .05 Hz (3 CPM) are shown in Figure 6. The cardiovascular responses to the maximum +2 $g_z$ stress of the sinusoidally-varying load are qualitatively and quantitatively similar to the +2 $g_z$ sustained values presented previously. In general for the 1, 2, and 3 cycles per minute variations used in this study, the cardiovascular responses followed without appreciable lag. As mentioned previously, the details of the transient responses are beyond the scope of this report, but will be reported in a subsequent document.

The various cardiovascular responses were meaned throughout the test period and averaged over all dogs tested. Since the mean results showed no consistent trends with the rates of oscillation used in these studies, the responses were further averaged over the three oscillations and presented as a function of the mean g level (Figure 7) for the various test cases, i.e. oscillations between 0 to +2 $g_z$ have a mean of +1 $g_z$ and oscillations between +1 $g_z$ and +2 $g_z$ have a mean of +1.5 $g_z$. In Figure 7, mean aortic flow, stroke volume, peripheral vascular resistance, systolic and diastolic aortic pressure, and heart rate are presented as a function of the mean g level to which the animal was exposed during the test period, whether produced by tilt, or sustained or time-varying acceleration. The data was further divided into those cases in which the animal was horizontal and vertical with respect to earth gravity. The first bar of each physiological variable is the value obtained for all animals in the horizontal position averaged over all control periods (0 $g_z$). The data in column 2 consists of the average of +1 $g_z$ tilt, 0 to +1 $g_z$ sustained acceleration, and 0 to +2 $g_z$ sinusoidal oscillations at 1, 2, and 3 cpm (mean $g_z$ equals +1). In the third column, data are presented for the animal in the horizontal position and exposed
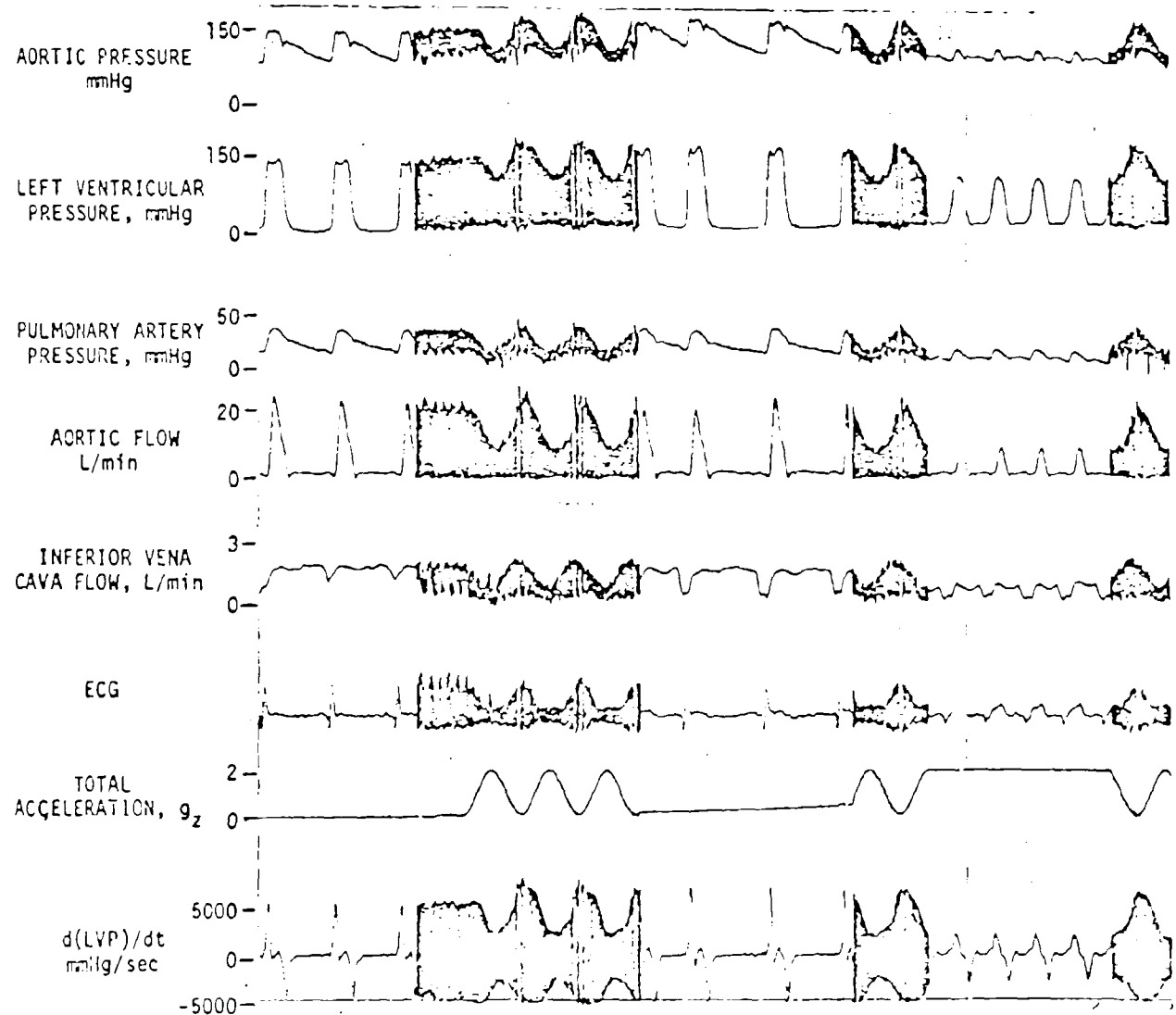
Fig. 6. Typical cardiovascular responses to 0 to +2 $g_z$, sinusoidally-varying acceleration at 0.05 Hz (5 min exposure).
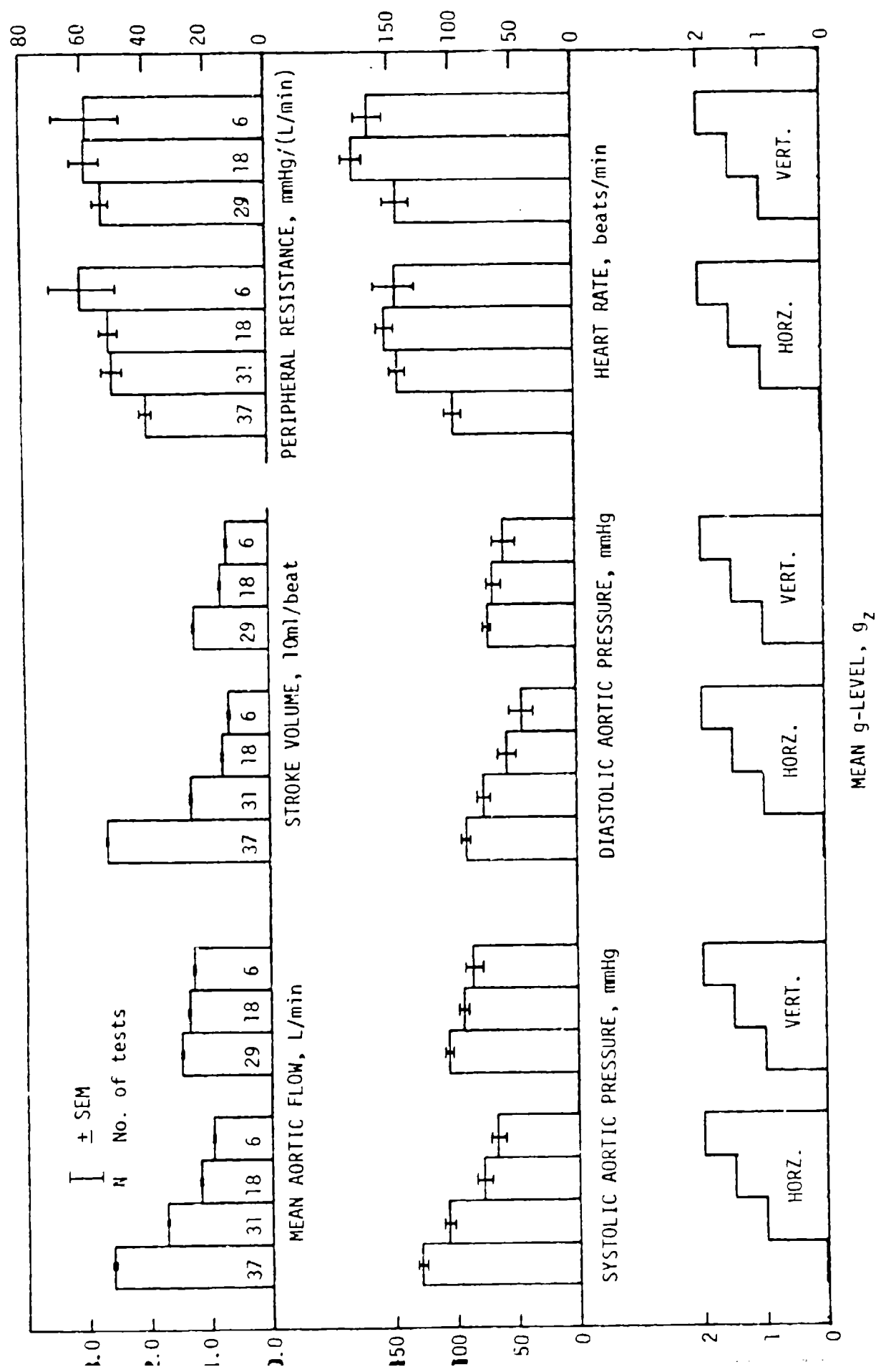
Fig. 7. Cardiovascular responses meaned over all animals and all tests as a function of mean g-level.

to sinusoidally-varying acceleration between +1 and +2 $g_z$ (a mean of +1.5 $g_z$).
For the animal in the same position a mean of +2 $g_z$ was produced by the 0 to
+2 $g_z$ sustained tests and these data are presented in the fourth column. In
the fifth column, data are presented for cases where the animal was in the
vertical position during control periods (a mean of +1 $g_z$). In the sixth
column, the mean g level is +1.5 and consists of those tests in which the animal
restraint was allowed to align itself with the resultant acceleration vector
and the g levels were sinusoidally varied between +1 and +2 $g_z$ at frequencies
of 1, 2, and 3 cycles per minute. In the last column, results are presented
for the 2 g sustained tests in which the animal restraint was initially vertical
and allowed to align itself with the resultant acceleration vector (a mean of
+2 $g_z$ during the test period). Mean aortic flow, stroke volume, and aortic
systolic and diastolic pressure were found to decrease with increasing mean g
level for both the horizontal and vertical cases. Generally, the decreases for
the horizontal cases were steeper than those for the vertical cases. The trend
in the data of heart rate and peripheral vascular resistance was an increase for g
levels above 0 g. However, no consistent trend was observed for these two
variables for the mean g levels of 1, 1.5, and 2, nor were there consistent
changes between the horizontal and vertical case. Of all the variables measured,
stroke volume again showed the most consistent trend as a function of mean g
level for both the horizontal and vertical cases. A comparison of the other
horizontal to vertical variables for identical g stress indicates both a vari-
ability in control and subsequent test values; the principal reason for presenting
the data in separate fashion.

## DISCUSSION AND CONCLUSIONS

As stated previously, the purpose of this study was to quantify mean
cardiovascular changes as a function of sustained and slowly-varying,

sinusoidal acceleration.  All of the cardiovascular responses measured in these studies were qualitatively and quantitatively similar for the 0 to +1 $g_z$ tilt and 0 to +1 $g_z$ centrifugation tests.  Stroke volume, mean aortic flow, systolic, diastolic and mean aortic pressures, right ventricular systolic pressure, and left ventricular dP/dt decreased from control.  Heart rate and peripheral vascular resistance increased.  All variables which decreased their values from control for the +1 $g_z$ sustained tests decreased their values further for the +2 $g_z$ tests.  However, heart rate and peripheral vascular resistance which increased from control for the 0 to +1 $g_z$ tests showed no further significant increase for the 0 to +2 $g_z$ test.

When the animals were exposed to a +2 $g_z$ stress after a +1 $g_z$ control period (produced either by centrifugation or orthostasis), the responses were less consistent.  Some of the variability in the responses is most probably due to the long period in which +1 $g_z$ was produced by maintaining the animal vertical prior to the test.  This long control period was necessitated by the centrifuge start-up procedure for this particular experiment.  This variability, however, is not apparent in stroke volume, whose values were the same for all +1 $g_z$ as well as +2 $g_z$ loadings.  In fact, stroke volume was the only cardiovascular variable whose change was consistent from test to test and dog to dog, and was the least affected by the way in which the acceleration stress was produced, i.e. tilt or centrifugation.  The consistency of the stroke volume response is extremely interesting especially in view of the lack of consistency in variables such as left and right ventricular end diastolic pressure which might be thought to indicate changes in stroke volume responses.  Although, not nearly as consistent as stroke volume, mean aortic flow and left ventricular dP/dt did show similar trends.  Systolic, diastolic and mean aortic pressures showed considerably more variation in their responses, especially the +1 $g_z$ control response produced by the long period of orthostasis.  To this extent, the aortic pressure variables

may be considered as better indicators of the stress state of the animal than stroke volume or mean aortic flow. It does appear that the combined stress of centrifugation following the prolonged vertical control periods resulted in a more stressed animal preparation for the +2 $g_z$ acceleration loading.

When acceleration stress varied sinusoidally at approximately 1, 2, and 3 cycles per minute at the same peak to peak acceleartion amplitudes as those produced during the sustained tests, responses meaned over the test period were found to correlate with mean g level during the test period only, and not with the frequency of oscillation. Those variables which showed a lack of correlation were heart rate and peripheral vascular resistance. The decrease in mean aortic flow and aortic systolic and diastolic pressures, with increasing mean g level, were greater when the animal was in the horizontal position than the vertical position with respect to the earth's gravity. This consistent trend, which was not seen in the sustained data alone, may suggest a possible adaptation of the cardiovascular system to the orthostatic pre-load thereby reducing the degree to which the values fell during the +2 $g_z$ exposure. Stroke volume responses decreased nonlinearly with increasing mean g and were independent of whether the animal was horizontal or vertical.

Taken collectively, these results indicate that for sinusoidal acceleration of 1, 2, and 3 cycles per minute at amplitudes of 0 to +2 $g_z$ and +1 to +2 $g_z$, the cardiovascular system was capable of following with peak to peak responses equal to those obtained for sustained tests and with mean responses correlatable with the mean g level of the test.

B. Comparison of the Orthostatic ($+1 \, g_z$) Tolerance of Awake Canines to that of Normal and Cardiovascularly Deconditioned Humans

## INTRODUCTION

The cardiovascular responses of canines to various stresses have been used to evaluate human responses to similar stimuli. An obvious drawback to making comparisons between human and canine responses occurs when the stimulus is the gravity vector imposed along the $g_z$ axis of the subject. The normal weightbearing stance of the human, being in the $g_z$ axis and that of the dog in the $g_x$ axis, suggests that the human would have a greater orthostatic tolerance to $+1.0g_z$ than would the canine. Human orthostatic tolerance to 1.0g changes however, whenever the normal gravity stimulus incurred in daily activity is changed. Spaceflight or the simulated weightlessness of bedrest or water immersion has been shown to induce cardiovascular responses to lower body negative pressure (LBNP), tilt, or orthostasis that vary substantially from "normal" responses (Miller, et al. 1964; Graveline, 1962; Goodall, et al. 1964; Wolthius, et al. 1974; Melada, et al. 1975; Hoffler and Johnson, 1975). Because tests following bedrest or water immersion sessions were originally performed on semi-immobile persons who were not getting normal amounts of daily exercise, further tests were done in which various exercise regimens were added to the "weightless" condition. The results of these studies indicated that exercise alone could not restore the "normal" response to orthostatic loading (Graveline, 1962; Vallbona, et al. 1965; Miller, et al. 1965; Vogt, 1966).

The present study was performed to compare the responses of chronically instrumented awake canines to tilt with those from existing human studies under reasonably similar experimental protocols in which the following subjects were used (1) healthy, normally active (hereinafter referred to as "normal") humans, (2) cardiovascularly deconditioned humans, and (3) cardiovascularly deconditioned humans-plus-exercise.

BACKGROUND

## Normal Human Subjects

The responses of normal humans to tilt from the horizontal to vertical
position has been studied with conflicting results. The common variables mea-
sured are, normally, systolic and diastolic blood pressures, heart rate and
sometimes cardiac output. Typically, heart rate increases with tilt, and stroke
volume decreases, combining to give a net decrease in cardiac output, but the
blood pressure responses are not predictable. Work done by Vallbona, et al.
(1965) showed one group of subjects (six subjects, 8 control and 8 test readings
each) to mildly increase both systolic and diastolic blood pressure (+3%) with a
mild decrease in heart rate (-6%) after four minutes of 70° tilt. A second group
of subjects (four subjects, ~ 40 sets of tests each) in the same study showed an
appreciable increase in systolic (+15%) and diastolic (+30%) blood pressures with
a 35% increase in heart rate when averaged over a 15 minute period of 70° tilt.
Musgrave, et al. (1971) using five normal subjects (~ six sets of tests each)
found both systolic (-8%) and diastolic (-4%) blood pressures to decrease while
heart rate rose (+20%) when averaged over 15 minutes of 70° tilt. Stegemann,
et al. (1975) using four nonathletic subjects (~ ten sets of tests each) showed
no change in systolic blood pressure with ten minutes of 70° tilt while diastolic
blood pressure and heart rate showed average increases of 20% and 40% respectively.
Melada, et al. (1975), with six subjects and three sets of tests each, found mean
aortic pressure to decrease slightly (-10%), while heart rate increased (20%),
stroke volume decreased (-50%), cardiac output decreased (-30%), and systemic
vascular resistance increased (+45%) during ten minutes of 60° tilt.

Even though systolic and diastolic blood pressure exhibited no predictable
behavior in the above studies, pulse-pressure did appear to consistently decrease,

sometimes dramatically, before syncope occurred. Subjects suspected of intolerance to orthostatic loading also exhibited fluctuations in their ability to maintain sufficient blood pressure. Some combination of all of the above factors has been sought to quantify a subject's tolerance to orthostatic loading. The most direct and meaningful of these being total peripheral resistance which has the drawback of requiring invasion of the vascular system for accurate, continuous measurement.

In an attempt to quantify the tolerance of subjects to tilt, Burkhart and Kirchoff (1966) proposed an emperical non-invasive orthostatic index which incorporated ratios of horizontal and vertical values of systolic and diastolic blood pressures and heart rate as well as the standard deviations in each variable taken over the vertical test period only:

$$O.I. = \frac{\text{systolic AP (H)}}{\text{systolic AP (V)}} \times \frac{\text{diastolic AP (V)}}{\text{diastolic AP (H)}} \times \frac{\text{HR (V)}}{\text{HR (H)}} \times 1/3 \sqrt{\Sigma(S.D.)^2} \text{ (vertical case)}$$

From measurements made on 500 subjects they found a mean orthostatic index of 12.4 $\pm$ 5.1 and concluded that as the index increased, the subjects' orthostatic tolerance decreased.

## "Weightless" Human Subjects

The weightless condition has been simulated by periods of bedrest in the range of 3 to 30 days or by periods of water immersion of several hours. Generally, cardiovascular responses to tilt or LBNP were measured in the subjects prior to the simulated weightlessness, at some time during the weightless period and at the end of the period. The results reported from the deconditioned subjects appear to be more uniform than from the normal controls. For example, Stegemann, et al. (1975) tilted four nonathletic subjects both pre and post six hours of water immersion, and found a greater increase in heart rate with the

post-immersion test (+80% post-immersion as compared to +60% pre-immersion tilt) as well as a decreased systolic aortic pressure (-10% vs. 0% pre-immersion) and a less increased diastolic pressure (+10% vs. +20% pre-immersion). In an accompanying series of tests on non-athletes, immersed in water for six hours but doing intermittent exercise, Stegemann found essentially the same results except that in the immersed, exercising non-athletes, systolic pressure did not decrease. Miller, et al. (1964) found an increase in orthostatic heart rate, >10% loss of blood volume, and evidence of postural hypotension following four weeks of bedrest. Graveline, 1962, found aortic systolic pressure to decrease and diastolic pressure to increase, resulting in reduced pulse pressure in each of five subjects over 10 minutes of 90° tilt following six hours of water immersion. Vogt (1966) found the fractional increase in heart rate to significantly increase (.53 to .81) following 10 days of bedrest in 11 subjects undergoing 70° tilt for 20 minutes. The same subjects showed corollary decreases in pulse pressure, and slope of the mean pressure with respect to time. Melada, et al. (1975) found tachycardia to be increased after ten minutes of tilt following bedrest, but stroke volume dropped 50% in both normal and bedrest tilt subjects. Peripheral resistance, which increased 45% in normal subjects following tilt, was increased only 20% in bedrest subjects, suggesting decreased vascular responsiveness with bedrest. Ghista, et al. (1976) in 20 minute LBNP sessions (-50 mmHg) on eight female bedrest (14 days) subjects found differences in the control states as well as in the response to LBNP. In all subjects, control stroke volume was decreased (-10% to -36%) and control total peripheral resistance was increased (+15% to +63%). With the LBNP testing, heart rate increased more after bedrest than before, and increases in total peripheral resistance were considerably lower.

Following an actual weightless period, Hoffler and Johnson (1975) evaluated the responses of Apollo crewmembers to 15 minutes of gradual LBNP stress (-8 to -50 mmHg) and/or 5 minutes of orthostasis both pre- and post-flight. The duration of weightlessness varied with the mission (from 6 to 12 days) and the weightlessness itself varied since some missions included lunar landings and some did not. Neverthless, the results of this study indicated that a reduction in orthostatic tolerance is a consequence of space flight exposure. Aortic systolic, diastolic, and pulse pressures were decreased as was total peripheral resistance during immediate post-flight evaluations using LBNP or orthostasis. Post-flight changes in leg volume during LBNP were equal to or less than those seen during pre-flight evaluations while body weight, resting calf girth, supine leg volume, and cardiothoracic ratios were all diminished post-flight.

Generally, the deconditioned response to passive tilt or LBNP, when compared to the normal response, can be characterized by increased heart rate and depressed aortic pressure (systolic, diastolic, pulse) indicating a deterioration of the subject's ability to tolerate orthostatic loading. To quantify the effects of weightlessness on orthostatic tolerance, Stegemann, et al. (1975) applied a modified version of the Burkhart and Kirchoff index to their group of tilt subjects both before and after six hours of inactive water immersion and found the group before to have an orthostatic index of $\sim 12 \pm 3$ (S.E.M.) increasing to $\sim 31 \pm 12$ (S.E.M.) following immersion. The two sets of data from the Vallbona, et al. (1965) study, where the first group was tested before and after 3 days of bedrest and the second group tested before and after 14 days of bedrest, has been analyzed for the present study using Burkhart and Kirchoff's original formula, to determine each sets' orthostatic index. The first group had an orthostatic index of $3.9 \pm 2.6$ (S.D.) before bedrest which increased to $4.4 \pm 1.5$ (S.D.) following three days of bedrest. The second group had an initial index of $6.4 \pm 2.4$ (S.D.) increasing to $9.7 \pm 3.6$ (S.D.) following 14

days of bedrest. In all cases the index was found to increase with cardiovascular deconditioning.

## Canines (Anesthetized)

Nutter, et al. (1969) measured the cardiovascular responses of anesthetized, chronically instrumented canines to 15 minutes each at increasing levels of lower body negative pressure (-30, -60, and -90 mmHg). They found that the graded decreases in left ventricular end diastolic volume produced by the LBNP resulted in significantly, and essentially linear, decreases in left ventricular systolic pressure (-6, -14, and -28% from control), maximum dp/dt (-4, -17, -53%) stroke volume (-18, -37, and -57%) and various derived parameters. Contractility as measured by the ratio of the maximum time derivative of left ventricular pressure to instantaneous pressure or by the ratio of the maximum time derivative of aortic flow to peak aortic flow was not found to vary significantly. Heart rate did not change in response to the increases in LBNP, probably due to its high average control value of 156 ± 34 b/min resulting from the anesthetized condition of the animal.

## Canines (Awake)

Studies of the responses of awake canines to tilt could not be found in the literature; a major reason for initiating the present study. The responses of awake, chronically instrumented canines to five minutes of vertical (90°) tilt is presented in this study for comparison with the anesthetized canines and with those of the above cited normal and cardiovascularly deconditioned humans when possible. The comparison will be made on the basis of changes in measured variables and the combination of those variables used to determine peripheral vascular resistance and the orthostatic index.

## METHODS

Twenty-two tests were conducted on nine days, using seven different animals. Each dog was chronically instrumented for continuous measurement of ascending aortic flow (Zepeda), left ventricular pressure (Konigsberg), circumflex coronary flow (Biotronex; plus occlusive zero). One of the animals was instrumented with an ultrasonic (L & M Electronics) flow probe on the inferior vena cava rather than a coronary flow probe. On the day of the experiment, the subject was tranquilized with INNOVAR-VET[t] @ 1cc/10 kg body weight IV and, under local anesthesia, both a femoral vein and an artery were cannulated for passage of manometer-tipped-catheters (Millar Instruments) into the left and right ventricles. After calibration of the implanted left ventricular gauge, via the acutely placed Millar gauge, the Millar gauge was backed into the aorta just outside the valve, and tied in for the remainder of the study. Next, the animal was restrained in the supine position for at least 20 minutes to establish a stable control. The animal was tilted to the vertical position over a five second period and all variables monitored for a five minute test period. Five minutes was chosen to compare with some of the previous human studies, and also because the animal appeared to stabilize in this time period. Following the tilt, the animal was returned to the horizontal position for a ten minute recovery period. Each animal was tested two or three times on the same day.

## RESULTS

Results from 14 tests on six days using chronically instrumented canines is presented. Data from the other three days was rejected since there was evidence that those animals had impaired cardiovascular systems and should be considered separately. Two of the three had no control left circumflex coronary

flow, very low stroke volume (14 ml) yielding low cardiac output (1.6 L/min) with an elevated systolic right ventricular pressure (>50 mmHg). The other animal also had low stroke volume (11 ml) elevated heart rate (125 b/min) low cardiac output (1.4 L/min), low aortic systolic (82 mmHg) and diastolic (45 mmHg) pressures with almost nonexistant systolic right ventricular pressure (5 mmHg) and was found to be unable to tolerate +2 $g_z$ in a later test. The response data of the first two was discarded based on the above and on pathological evidence of myocardial infarction occurring downstream of the implanted left circumflex coronary artery flow probe and occluder at some time (< 14 days) prior to the test. The inability of the third animal to maintain heart rate, flow or pressure at +2 $g_z$ made the +1 $g_z$ response questionable, particularly when viewed in light of his extremely low control (horizontal) values also. The other six dogs (14 tests) were judged to be normal both in control values and in their ability to respond to stress.

Typical responses of an awake, chronically instrumented canine to 5 minutes of 90° tilt are shown in Fig. 1, the dog in this case being that animal in which inferior vena cava flow was substituted for coronary flow. Obvious responses are tachycardia, reduced (and steadily diminishing) aortic and left ventricular diastolic pressure (not a consistent finding), decreased pulmonary artery systolic and diastolic pressures, decreased and diminishing peak aortic flow and stroke volume, decreased return of blood from the lower body segment as shown by decreased inferior vena cava flow, decreased maximum dp/dt and a change over the five minute test period in the ST segment of the ECG. Figure 2 shows five minute averages over all animals for control and test periods with the ± standard error of the mean (S.E.M. = $\frac{S.D.}{\sqrt{n}}$). In all tests except one, both systolic and diastolic aortic pressures decreased, and in that case there

DOG: CHRONICALLY INSTRUMENTED, TRANQUILIZED, 5 MINUTE TILT
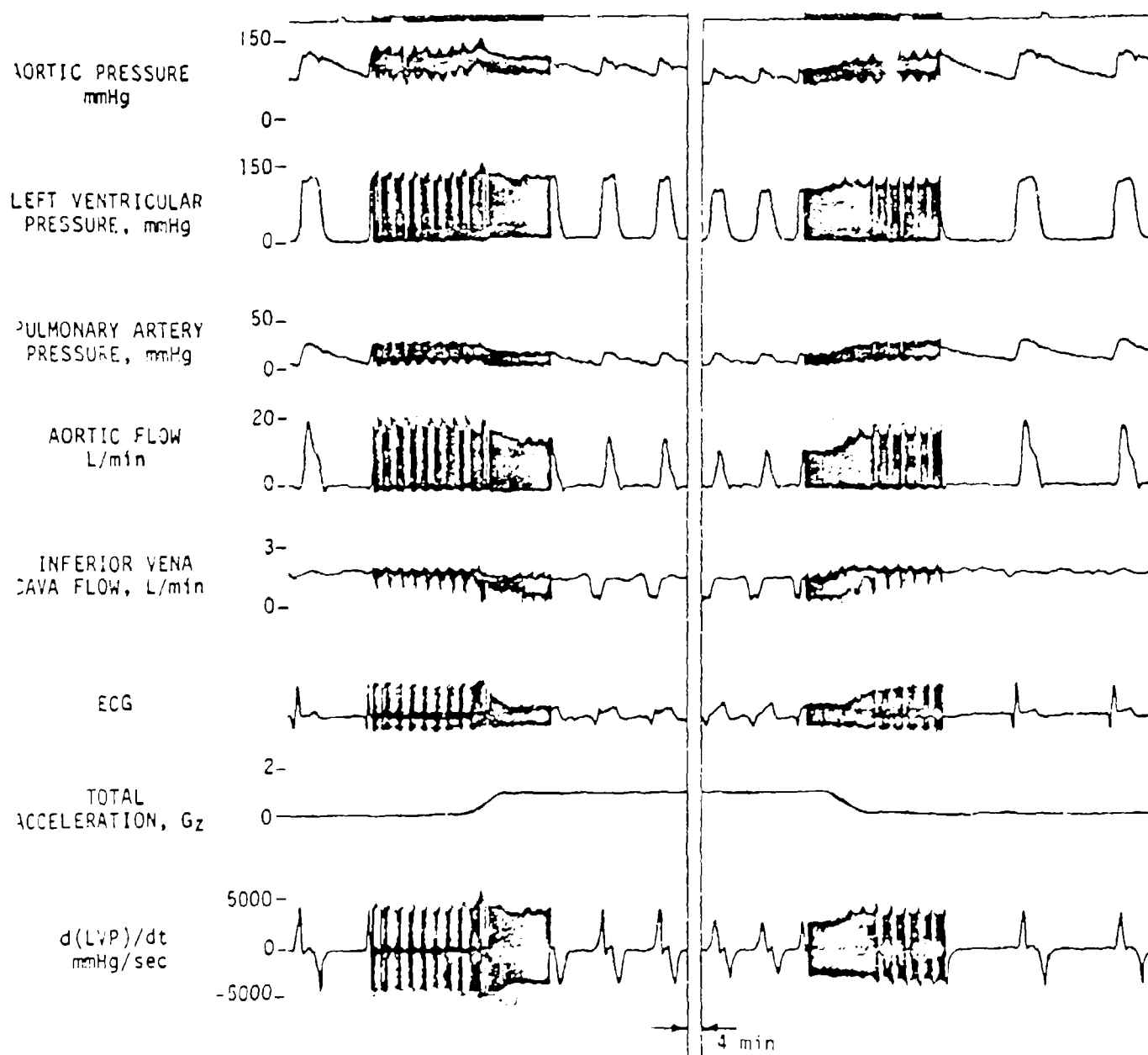


Fig. 1. Cardiovascular responses of an awake, but tranquilized, chronically instrumented dog to five minutes of vertical tilt.
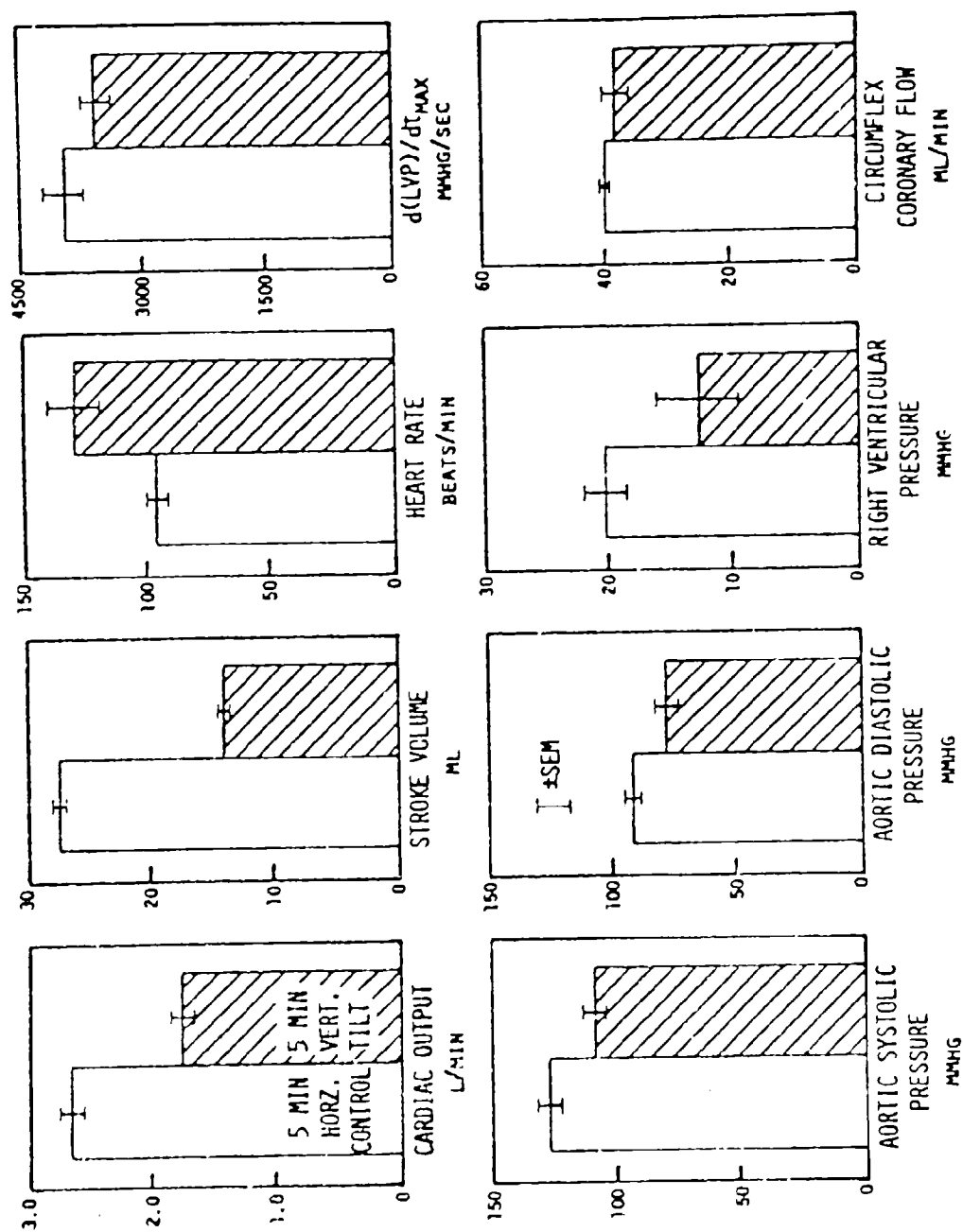
Fig. 2. Five minute averages of control (horizontal) and test (vertical) values ± S.E.M. for 14 tests on six awake, chronically instrumented canines.

was no change. In all tests, heart rate increased and stroke volume decreased which, when combined, showed a decrease in cardiac output in each case. Coronary flow showed a characteristic time variation; where the immediate response to tilt was increased coronary flow, followed by a decrement in flow over the remaining test period, with a net result of no appreciable change from control when averaged over the five minute test period. Maximum dp/dt consistently showed an initial short increase followed immediately by a decrease below normal that lasted throughout the test session for an average decrease of $-12.6 \pm 2.0\%$. Power density, the integrated plot of dLVP/dt vs LVP over each heart cycle showed approximately a 15% decrease over the test period. Left ventricular diastolic pressure decreased in 9 cases ($-2.0 \pm .5$ mmHg) and increased in the other four ($+3.7 \pm 1.9$ mmHg) with tilt for an average change of $-.2 \pm 1.0$ mmHg. ECG (sternal lead) showed initial changes with tilt that were attributed to the relative shift of electrode positions with respect to the heart, but also over the five minute test sessions the magnitude of the T segment was often seen to change with time. Systolic right ventricular pressures decreased in 8 of 10 cases, ($-40 \pm 18\%$) while diastolic right ventricular pressure increased in four cases, ($1.4 \pm .5$ mmHg) and decreased in six ($-2.4 \pm 1.0$ mmHg) for an average change of $-.9 \pm .8$ mmHg.

## Comparison of Results with Other Studies

Figure 3 is a comparison of the effects of vertical tilt on the awake canines of this study with normal humans both before and after some period of cardiovascular deconditioning. The anesthetized canine study did not include aortic pressure measurement, and that, plus the high control heart rate, precluded comparison with the human studies. The results shown are in terms of percentage change from control (horizontal) values. The question asked by the
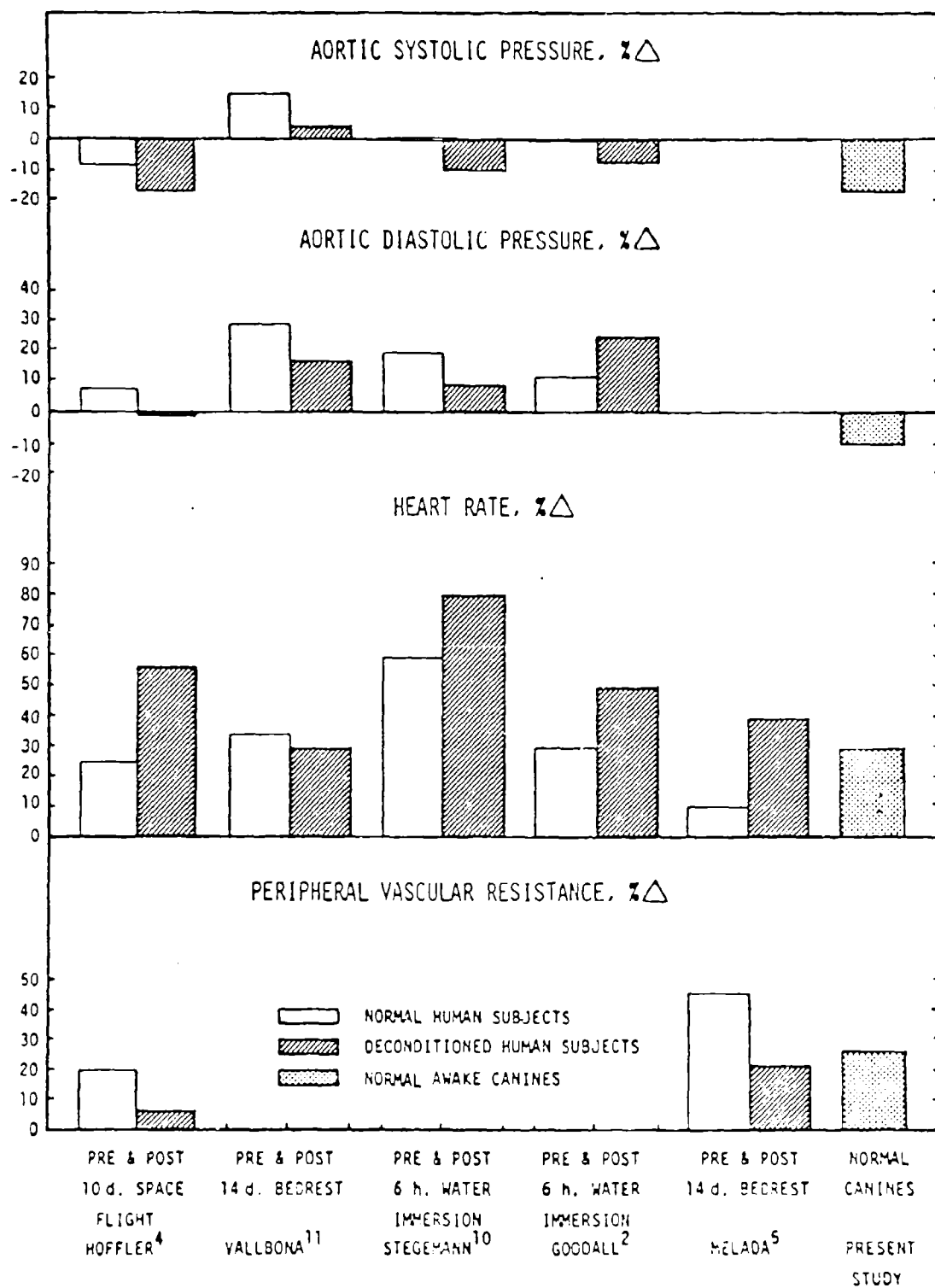
Fig. 3. Comparison of the cardiovascular responses of awake canines, normal humans and cardiovascularly deconditioned humans to the orthostatic stress of vertical tilt, LBNP or passive stand.

comparison is "To what degree are the responses of the normal dog to vertical tilt similar to those seen in comparable human studies?". The first overall observation is that at least in terms of those variables shown, there is no great difference in any of the three groups of subjects. Aortic systolic pressures are all ± 20% of their control values, aortic diastolic pressures are all ± 30% of control values, heart rate ranges from +10% to +80% averaging ∿ 35% for all groups, with peripheral vascular resistance showing increases of 5% to 40% from control.

Differences between the three groups, particularly between normal human subjects and the same subjects following cardiovascular deconditioning, are evident. Following any of the deconditioning procedures, the human systolic aortic pressure responses to orthostatic stress were less than those for the normal subjects. One showed less of an increase, while the other three decreased; in some cases the decrease approached that measured for the awake dog. In three of the four human cases, the diastolic aortic pressure response to orthostatic stress is seen to decrease with deconditioning. The deconditioned heart rate increase is above normal in four of five cases, some below, some above and some in the range of the canine response. The increase in peripheral vascular resistance shown by the normal human in response to tilt is seen to be less in both cases following deconditioning; in one case the normal, and in the other the deconditioned, response was similar to that of the dog.

The orthostatic index was calculated for all studies in which the necessary information was given. These data are presented in Fig. 4 for normal humans, humans following some experimentally induced amount of cardiovascular deconditioning and normal canines. In all cases, those subjects experiencing cardiovascular deconditioning showed an increased orthostatic index over their own
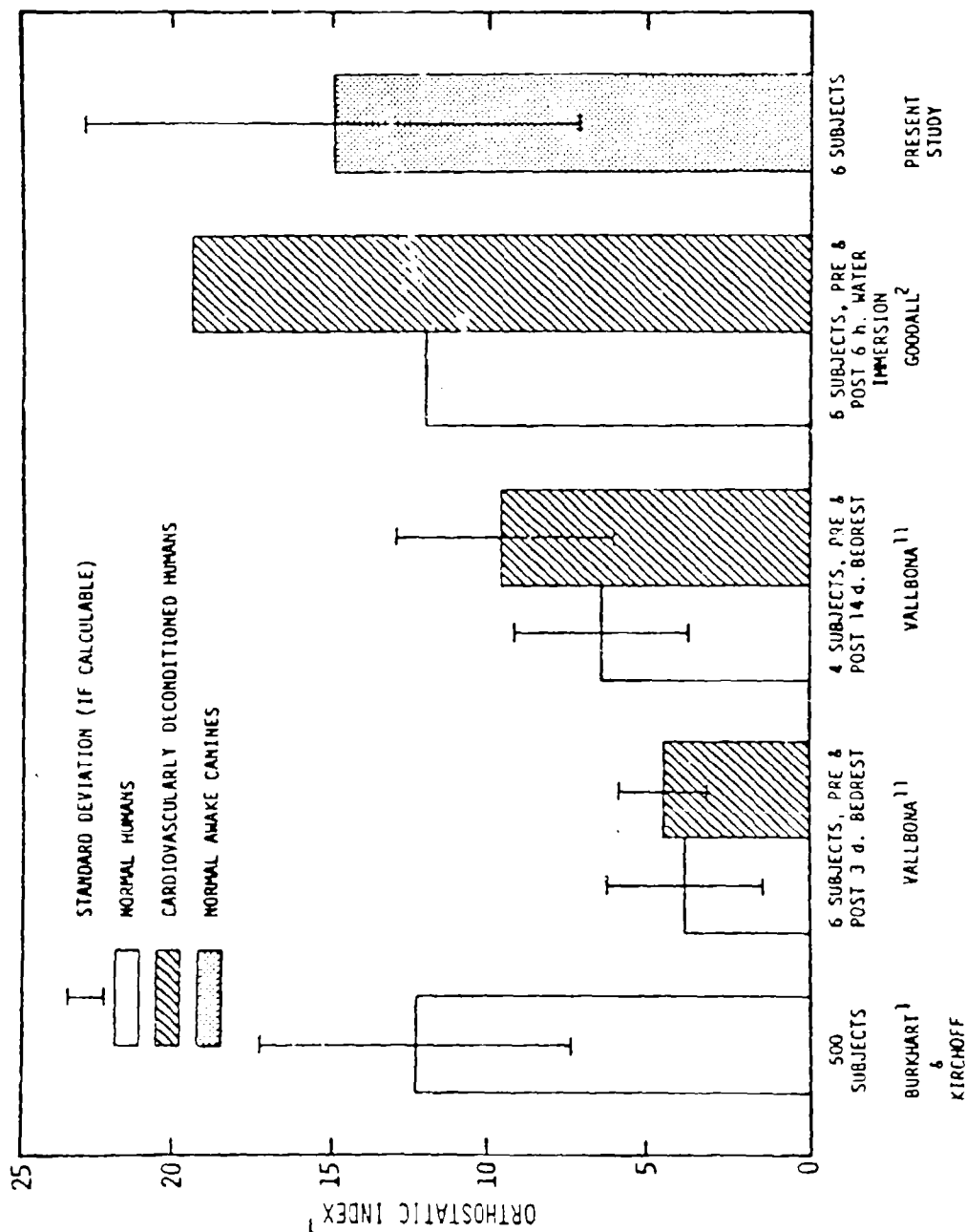
Fig. 4. The cardiovascular responses of normal humans, cardiovascularly decon-
ditioned humans and awake canines to vertical tilt as indicated by the
orthostatic index of Burkhart and Kirchoff.

normal index. The range of canine indices was from 4.8 to 27.7 with an average of 14.9 ± 7.9 (S.D.) indicating a variability among subjects that paralleled the values calculated for the human subjects. The mean value for the canines indicates a system that is slightly less tolerant to tilt than the normal human system, even though it still lies well within the range of the human response as indicated by the standard deviation in the Burkhart and Kirchoff study.

## Discussion

The variability of the normal human blood pressure response to orthostatic loading makes comparison with the normal canine response difficult. While normal humans may show increases or decreases in aortic systolic and/or diastolic pressure, the dog generally responds with a decrease of approximately 15% of both systolic and diastolic pressure. Heart rate responses are similar in that both normal humans and canines show increases in the range of 35%. The consistent finding in each canine studied was the decrease in stroke volume which averaged 40% of control. This value does compare with that of normal humans subjected to LBNP as presented in the Wolthius review article of 1974, in which three studies are cited where stroke volumes declined by 30 to 50% with varying LBNP levels. The 1975 tilt study of Melada also shows a 40% reduction in stroke volume for both normal subjects and the same subjects after 14 days of bedrest. The Apollo spaceflight data showed a decrease in stroke volume of 33% for pre-flight LBNP of -50 mmHg and 44% post-flight response to the same stimulus. The anesthetized canine study of Nutter (1969) also showed a decrease in stroke volume of 37% at an LBNP of -60 mmHg. All of the above combine to indicate that there may be a general cardiovascular response to $\sim + 1g_z$ in which stroke volume will drop by $\sim$ 40%, regardless of the type of subject. The mechanism of adjustment to a new steady state following this common drop will depend on the type of subject, be it normal human, deconditioned human, awake or anesthetized canine.

Changes in other responses of subjects after deconditioning are interest-
ing in that the deconditioning sometimes produces a response more like that of
the canine. For example, the 45% increase in peripheral resistance shown by
normal subjects in the Melada (1975) study dropped to a 20% increase after bed-
rest where the normal dog shows an increase of $\sim$ 25%. Another example is the
orthostatic index of canines which appears to be on the high side of the normal
human index and more in line with the deconditioned human index.

It must be noted however that no animals showed signs of syncope except
that animal which could not tolerate $+2g_z$, this may be due however to the limited
duration (5 min) of the tests performed. Another interesting fact is that a
later set of tests in which a canine is restrained in a "mummy" type enclosure
with the feet tucked up against the abdomen has shown a different type of re-
sponse from the lightly restrained animals of the present study.

Taken all together, the results of the present study indicate that the
response of the normal awake canine to orthostatic loading along the spinal
axis is quite similar to that of normal human subjects, but with enough differ-
ence to indicate that the canine might also be studied as a surrogate for man
in a non-extreme state of cardiovascular deconditioning.

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## C. Comparison of Cardiovascular Responses in Canines Restrained Vertically and Horizontally to $g_z$ Sinusoidal Vibration (2-20 Hz)

### INTRODUCTION

Considerable effort in the past was devoted to evaluating the change in mean aortic flow of animals restrained vertically as a function of whole body $g_z$ vibration at frequencies of 2-20 Hz. Results of this study showed that when mean aortic flow was plotted against the force transmitted to the animal at each frequency, it was found to increase linearly with increasing force. To delineate the influence of $+g_z$ orthostasis on these data, studies were performed on animals restrained horizontally with respect to earth gravity and exposed to the same vibration protocol as those animals restrained vertically.

### METHODS

Canines (16 to 22 kg) were chronically instrumented with electromagnetic flow cuffs (Zepeda) around the ascending aorta, right and left atrial cathethers and in some cases left ventricular and/or aortic pressure gauges (Konigsberg). After a minimum of ten to fourteen day post operative period, each animal was brought to the laboratory for transducer calibration and then later for study.

The electromagnetic flow transducers were calibrated using indocyanine green dye dilution techniques. The animals were normally placed in a sling and lightly restrained for this procedure. The vertical vibration system which was used in previous studies is shown in Figure 1 for comparison with the horizontal system used in these studies. In the previous studies the animal was restrained vertically with respect to earth gravity and vibrated along the $g_z$ axis at acceleration amplitudes of $\pm 1$ g and frequencies from 2 to 20 Hz. In these studies the animal was restrained horizontally with respect to earth gravity (Figure 2) and exposed to the same vibration protocol used for the vertical studies.
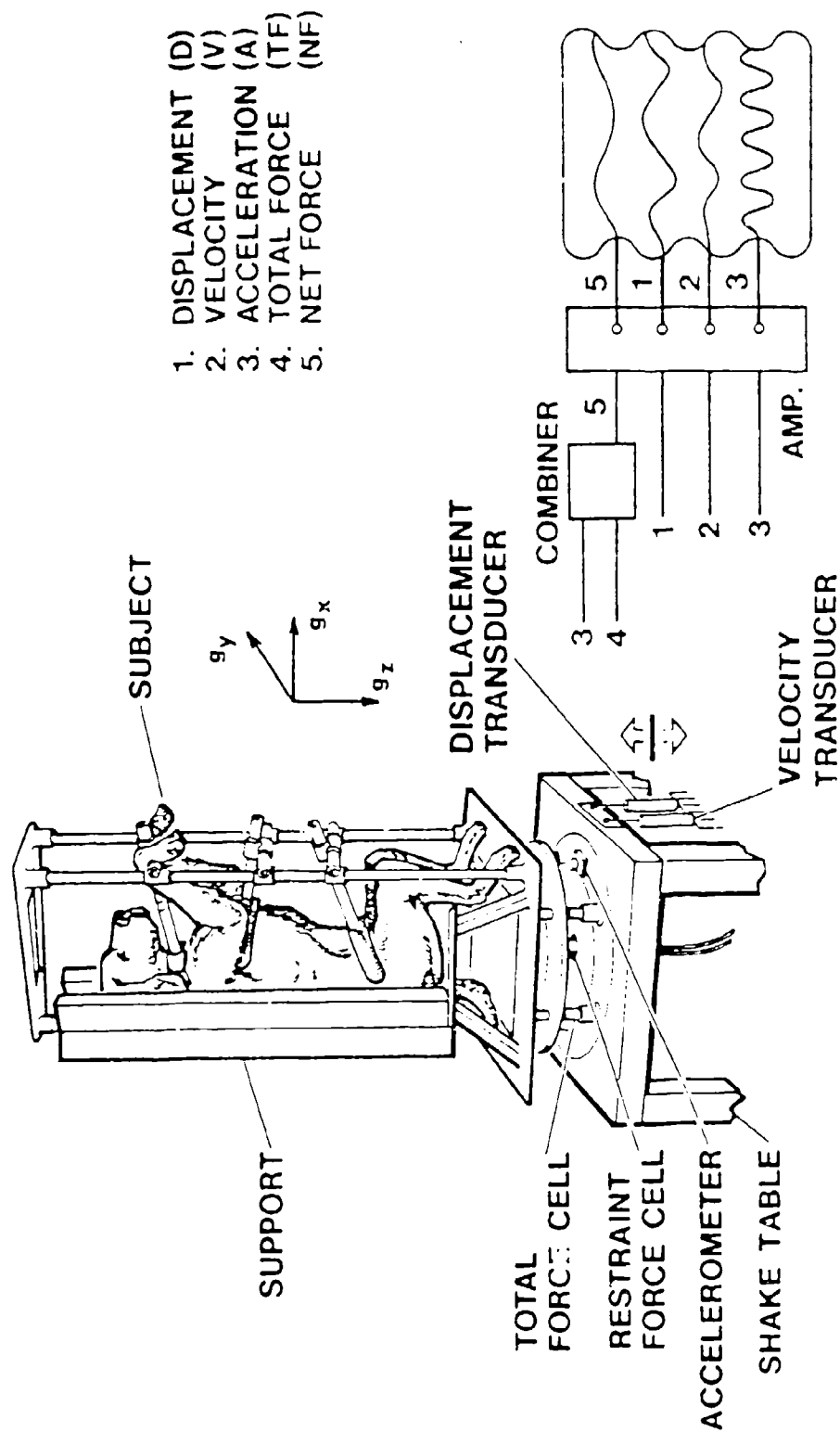
Fig. 1. Vertical Vibration Exciter.

# HORIZONTAL VIBRATION EXCITER



$g_x$

$g_y$

$g_z$

4. FORCE CELLS (3)

3. ACCELEROMETER

2. VELOCITY TRANSDUCER

PISTON

NYLON
BEARING

BEARING

1. DISPLACEMENT
TRANSDUCER

1. DISPLACEMENT (D)
2. VELOCITY (V)
3. ACCELERATION (A)
4. TOTAL FORCE (TF)
5. NET FORCE (NF)

3
4

COMBINER

5

5
1
2
3

AMP.
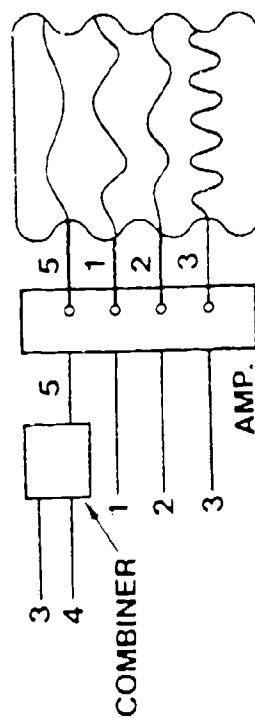
NOTE:
NF · TF·KA
K · MASS OF RESTRAINT SYSTEM

Fig. 2. Horizontal Vibration Exciter.

Six studies were conducted using four animals. Each study was done with the subject totally awake, and begun after a baseline period of 30 minutes was completed. The vibration parameters consisted of the sequential application of $\pm 1$ $g_z$ acceleration for the following frequencies: 2.3, 3, 4, 5, 6, 7, 8, 10, 12 and 20 Hz. Each test consisted of 30 seconds of $\pm 1$ $g_z$ at one of the frequencies followed by one minute recovery and one minute control periods. One of the animals was studies three times; first in the horizontal position, nine days later in the vertical, and four days after that in the horizontal again.
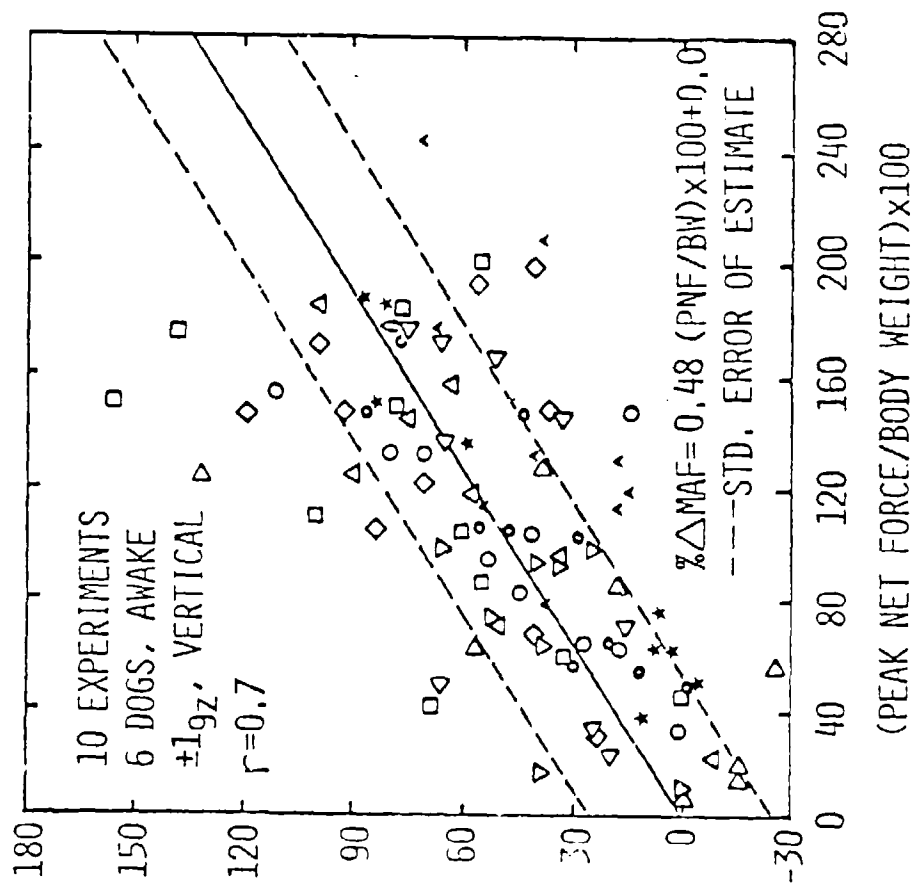
## RESULTS

Percentage change from control (no vibration) of mean aortic flow is plotted versus the peak force transmitted (PNF) to the animal during each horizontal vibration exposure in Figure 3a. The transmitted force data is normalized with respect to the animal's body weight (BW). Corresponding data from the vertical studies done previously is shown in Figure 3b. A combination of the results of the two studied is shown in Figure 4 without data points for purposes of comparison. The scatter in the data is notable as indicated by the standard error of the estimate. However, the rate of increase of mean aortic flow as a function of PNF/BW was considerably less when the animal was restrained horizontally with respect to earth gravity than for the animals restrained vertically. Responses of the animal that was run twice in the horizontal and once in the vertical position were qualitatively and quantitatively similar to the corresponding mean values shown in Figure 4.

A summary of the responses of the horizontal and vertical experiments is presented in Table I. The most striking difference, other than the relative slopes of the data, between the two experiments is the difference in the control stroke volume for the vertical subjects, proximately 40% less than for the animal restrained

**Graph a (left):**

PERCENT CHANGE MEAN AORTIC FLOW

180 — 150 — 120 — 90 — 60 — 30 — 0 — -30

6 EXPERIMENTS
4 DOGS, AWAKE
±1g$_z$, HORIZONTAL
r=0.5
%△MAF=0.12(PNF/BW)x100+11.7
——STD. ERROR OF ESTIMATE

0  40  80  120  160  200  240  280

(PEAK NET FORCE/BODY WEIGHT)x100

a

**Graph b (right):**

180 — 150 — 120 — 90 — 60 — 30 — 0 — -30

10 EXPERIMENTS
6 DOGS, AWAKE
±1g$_z$, VERTICAL
r=0.7
%△MAF=0.48(PNF/BW)x100+0.0
——STD. ERROR OF ESTIMATE

0  40  80  120  160  200  240  280

(PEAK NET FORCE/BODY WEIGHT)x100

b

Fig. 3. Percentage change in mean aortic flow as a function of peak net force/body weight over the g$_z$ vibration range of 2-20 Hz.
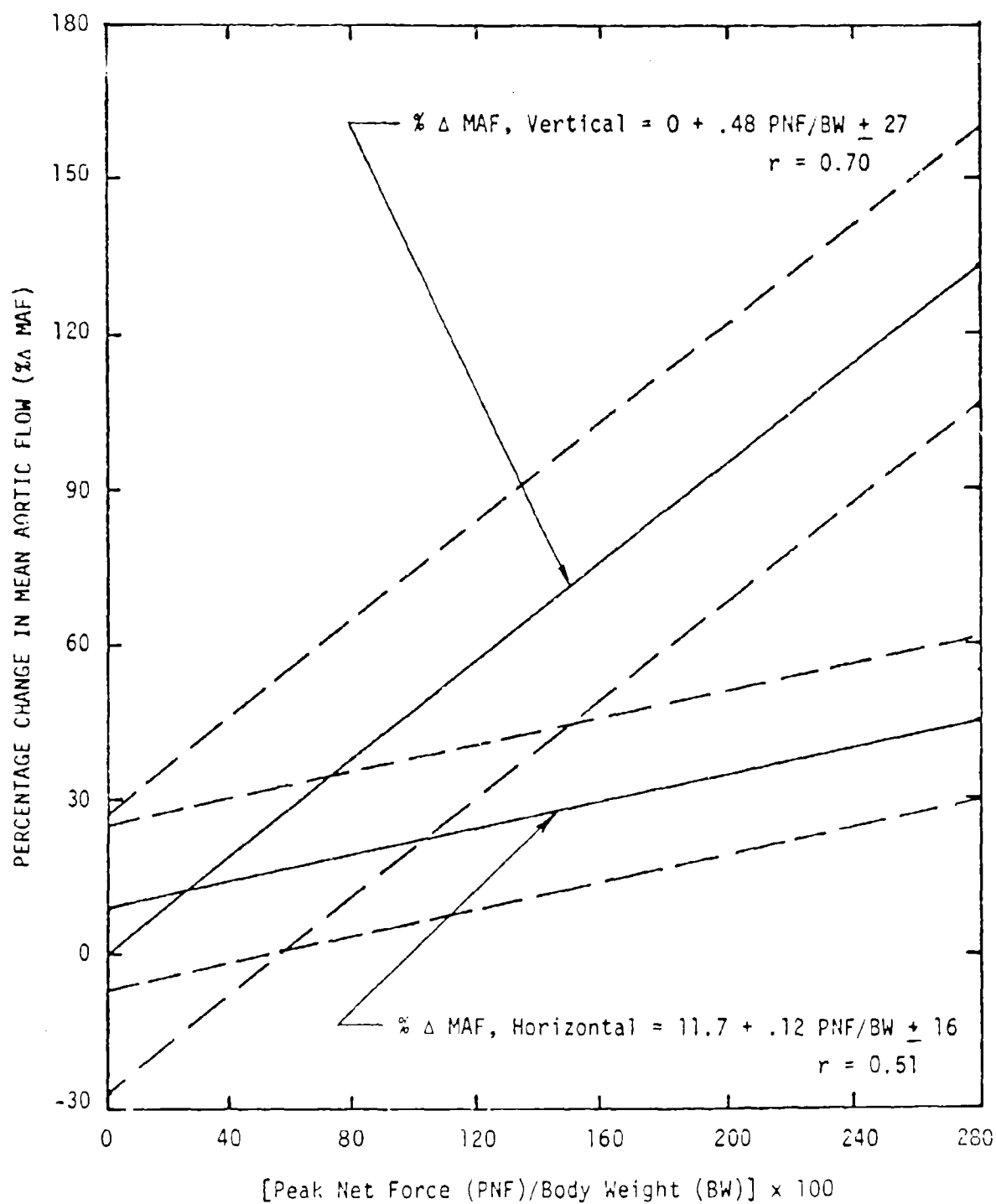
Fig. 4. Comparison of percentage change in mean aortic flow vs peak
net force/body weight for animals restrained horizontally
and vertically during $g_z$ vibration.

Table I

## A SUMMARY OF CARDIOVASCULAR RESPONSES TO
## HORIZONTAL AND VERTICAL $G_z$ WHOLE BODY VIBRATION

| Vertical | Horizontal |
|---|---|
| 11 Awake Studies | 6 Awake Studies |
| $\%\Delta$ MAF vs PNF/BW: | $\%\Delta$ MAF vs PNF/BW |
| $\%\Delta$ MAF = 0.0 + (.476) PNF/BW | $\%\Delta$ MAF = 11.7 + (.118) PNF/BW |
| S.E.E. = $\pm$ 26.7 $\%\Delta$ MAF | S.E.E. = $\pm$ 15.5 $\%\Delta$ MAF |
| Correlation Coefficient r = 0.70 | Correlation Coefficient r = 0.51 |

Range of Average Experimental Controls:

| Vertical | | | Horizontal | | |
|---|---|---|---|---|---|
| 2 Hz C | | 20 Hz C | 2 Hz C | | 20 Hz C |
| MAF 2.26 | → | 2.32 L/min | MAF 3.71 | → | 4.05 L/min |
| HR 136 | → | 140 beat/min | HR 151 | → | 158 beat/min |
| SV 13.1 | → | 15.4 ml/beat | SV 25.1 | → | 26.0 ml/beat |

Range of % Change With Vibration:

| Vertical | | Horizontal | |
|---|---|---|---|
| MAF | -30% to +150% | MAF | -3% to +82% |
| HR | -25% to +100% | HR | +2% to +70% |
| SV | -48% to +168% | SV | -10% to +32% |

Resonance:

| Vertical | Horizontal |
|---|---|
| 3 to 4 Hz @ 1.7 PNF/BW | 2 to 3 Hz @ 1.9 PNF/BW |

horizontally. Control heart rate for each group of animals was not considerably different. In both cases the heart rates were relatively high, probably due to the totally awake state of the animal even though previously adapted to the laboratory setting. Thus as a result of the reduced control stroke volumes, measured in the vertical case, the values of mean aortic flow were also less for control and never reached values as high as those measured for the horizontal case.

Another difference was in the range of responses shown by the vertical as opposed to the horizontal subjects. As evidenced in Table I, the subjects in the vertical position showed a much wider range of vibration-induced responses than did those in the horizontal. The whole body resonance for the two cases (as indicated by maximum transmitted PNF/BW over the frequency range studied) showed a slight difference, falling between 3 to 4 Hz for the vertical and between 2 to 3 Hz for the horizontal subjects.

The mean aortic flow responses were further examined to determine the relative contributions of changes in stroke volume and changes in heart rate that produced the measured responses. For the vertical studies the responses were found to fall into three separate categories: Category I was comprised of subjects who responded to increased peak force by increasing heart rate with no change in stroke volume, Category II subjects were opposite; they changed stroke volume with little or no change in heart rate while Category III subjects changed both heart rate and stroke volume by fairly equal amounts. It was generally determined that the control (pre-vibration) levels of heart rate appeared to indicate into which category the vibration-induced response would fall. Subjects whose control heart rates were less than 150 b/min fell mostly into Category I, those above 100 b/min fell mostly into Category II, while the subjects of Category III appeared to have no dependence on initial heart rate.

When the subjects for the horizontal experiments were examined for the changes in heart rate and stroke volume, it was found that in contrast to the vertical experiments, all increases were due mainly to increases in heart rate. Stroke volume did increase slightly during some of the vibration sessions but showed no appreciable dependence on the PNF/BW.

## DISCUSSION AND CONCLUSIONS

The principal finding of this study was the marked difference in MAF response to $g_z$ whole body vibration for canines in the vertical as compared to the horizontal position. The vertical subjects were shown to markedly increase MAF with increasing transmitted force (PNF/BW), while the horizontal subjects showed only a minor increase. The increases in MAF for the animals restrained vertically were produced in three distinct ways: one group of animals in which heart rate increased only, one group in which stroke volume increased only, and one group which used a combination of both. In constrast, the increases in MAF for the animals restrained horizontally were produced principally by increases in heart rate.

The other major finding was the difference in control (pre-vibration) stroke volumes between the two sets of subjects, the stroke volume for the vertical subjects being approximately 40% less than that of the horizontal subjects. The decreased control volumes observed for the vertical experiments are most likely a result of pooling of blood in the periphery due to the +1 $g_z$ orthostatic loading of the animal. Some of the scatter in the data for the vertical test is most probably due to the length of time the animal was vertical prior to the actual tests, which varied somewhat depending how well all systems functioned.

It appears that the combined stress of +1 $g_z$ orthostasis and $g_z$ vibration produces a more sensitive cardiovascular system responding with larger changes in mean aortic flow than those seen with $g_z$ vibration in the absence of orthostasis.

The mechanism responsible for this observation is not obvious. One possibility is that venous return is enhanced for those animals in the vertical position due to the one-way venous valves. Another possibility, is that the responses are primarily due to neural mechanisms activated more readily by vibration when the animal is restrained vertically; a mechanism known in the past to be highly responsible for changes seen in awake animals as compared to anesthetized animals who were restrained vertically and vibrated in the $+g_z$ axis (previous progress reports). In any event, the responses are sufficiently different to warrant further studies.

D. Acceleration Transmissibility of Internal Organs in Canines Exposed to Whole Body Vibration (2-12 Hz)

INTRODUCTION

In previous studies, whole body transmitted force has been shown to be an important parameter in characterizing the response of the cardiovascular system to whole body vibration. However, this parameter represents the integrated response of the various body subsystems, and does not provide information about the distributed nature of the vibration forcing function as it reaches the various body organs. Measurement of the specific response of individual body organs would presumably facilitate a more direct definition of the mechanisms by which vibration-induced cardiovascular pressure/flow changes are produced. In addition, knowledge of the distributed nature of the forcing function would provide valuable information for 1) the assessment of stress/strain levels generated in individual organs by exposure to whole body vibration, and 2) improved biomechanical modeling efforts. With this in mind, the studies reported here were initiated to measure the $g_z$ stress acceleration transmissibility of individual organ systems.

METHODS

Acutely instrumented canines were exposed to $g_z$ whole body sinusoidal vibration. Two vibration platforms were employed: a vertical vibration table on which the animals were restrained vertically and vibrated along their spinal axis, and a horizontal slip table on which the animals were restrained horizontally and vibrated along the spinal axis.

Measurements of the acceleration of internal body organs were made with miniature, single-axis, Konigsberg piezo-resistive accelerometers. Accelerometers were implanted on the heart (apex of the left ventricle), diaphragm (midline of abdominal surface) and sternum (subcutaneously on the sternal crest), so that their sensitive axis was parallel to the axis of vibration ($g_z$). The transducers

were given an absolute $\pm$ g calibration prior to implantation, and a relative
calibration after surgical closure by tilting the restrained animals from the
positive to negative $g_x$, $g_y$, and $g_z$ directions. Anatomical placement and
orientation was visually reconfirmed during post-experimental autopsy. The cali-
bration and alignment of the transducers for each preparation were readily
established by this technique. Included in a number of the preparations was the
acute placement of a Millar dual-sensor catheter tip pressure transducer through
a ligated branch of the subclavian artery proximal to the aortic arch. The
Millar transducer was adjusted so that the distal sensor was located within the
aortic arch, while the proximal sensor was open to the extravascular (thoracic)
space, thus enabling the simultaneous measurement of intravascular aortic
pressure and intrathoracic pressure from which transmural aortic pressure was
obtained. Surgical closure of all sites was effected prior to experimentation.
The animal preparation was anesthetized with Chloralose-Urethane, and maintained
on a respirator at all times.

The animals were exposed to a frequency range of 2-20 Hz and acceleration
amplitudes of 0.75, 1.0, and 1.25 $g_z$, for both vibration modes. An exposure
duration of 30 seconds at each vibration frequency was specified on the basis
of previous tests which established this duration to be sufficient to obtain
reliable results. When possible each preparation was run both horizontally
and vertically using the same protocol.

<center>RESULTS</center>

The transmissibility modulus (TM) of each organ is defined as the ratio of
the peak-to-peak acceleration measured by the accelerometer attached to the organ,
divided by the peak-to-peak amplitude of the measured table acceleration. The
transmissibility phase angle (TPA) is defined as the lag of the $+g_z$ organ accel-
eration peak behind the $+g_z$ peak of the table acceleration (in degrees of one

cycle). Analysis of the TM data presented must be tempered with the realization that, although the transducers were implanted in an orientation parallel to the $g_z$ direction, it cannot be said with certainty that this parallelism was maintained during vibration (i.e., that the transducers responded only to the $g_z$ component of induced acceleration, or that transducer motion was only in the z direction). On the basis of anatomical structure and restraints of the diaphragm and sternum sites, it can be reasonably assumed that, for the transducers mounted at these locations, the $g_z$ component constituted the major portion of the measured response. The possibility of heart motion (and therefore induced acceleration) in the lateral and transverse planes cannot be as easily ruled out, but there was some indirect evidence (visual observations in an open-chested dog) to support the contention that the measured heart acceleration was mainly a $g_z$ response. While absolute values of TM may be questioned, relative changes in TM over the frequency and g level range tested, for both horizontal and vertical modes, should provide insight into the distributed nature of the acceleration forcing function.

Examples of TM and TPA of the diaphragm, heart, and sternum as a function of frequency for one dog tested vertically and horizontally are shown in Figure 1 and 2 respectively. Normalizing absolute organ acceleration response by measured table acceleration yielded a close-fitting family of TM curves for the various g levels employed (measured values may differ somewhat from the less accurate values calculated from table displacement and frequency). Consequently, the TM of each organ is represented in Figures 1 and 2 by a single response curve, which is an average of the discrete g level curves. The TPA curves for each organ were found to be essentially independent of input g level and are therefore similarly represented by a single average response curve. The average deviation of individual data values for each curve shown are given by the "S.D. Average" range.

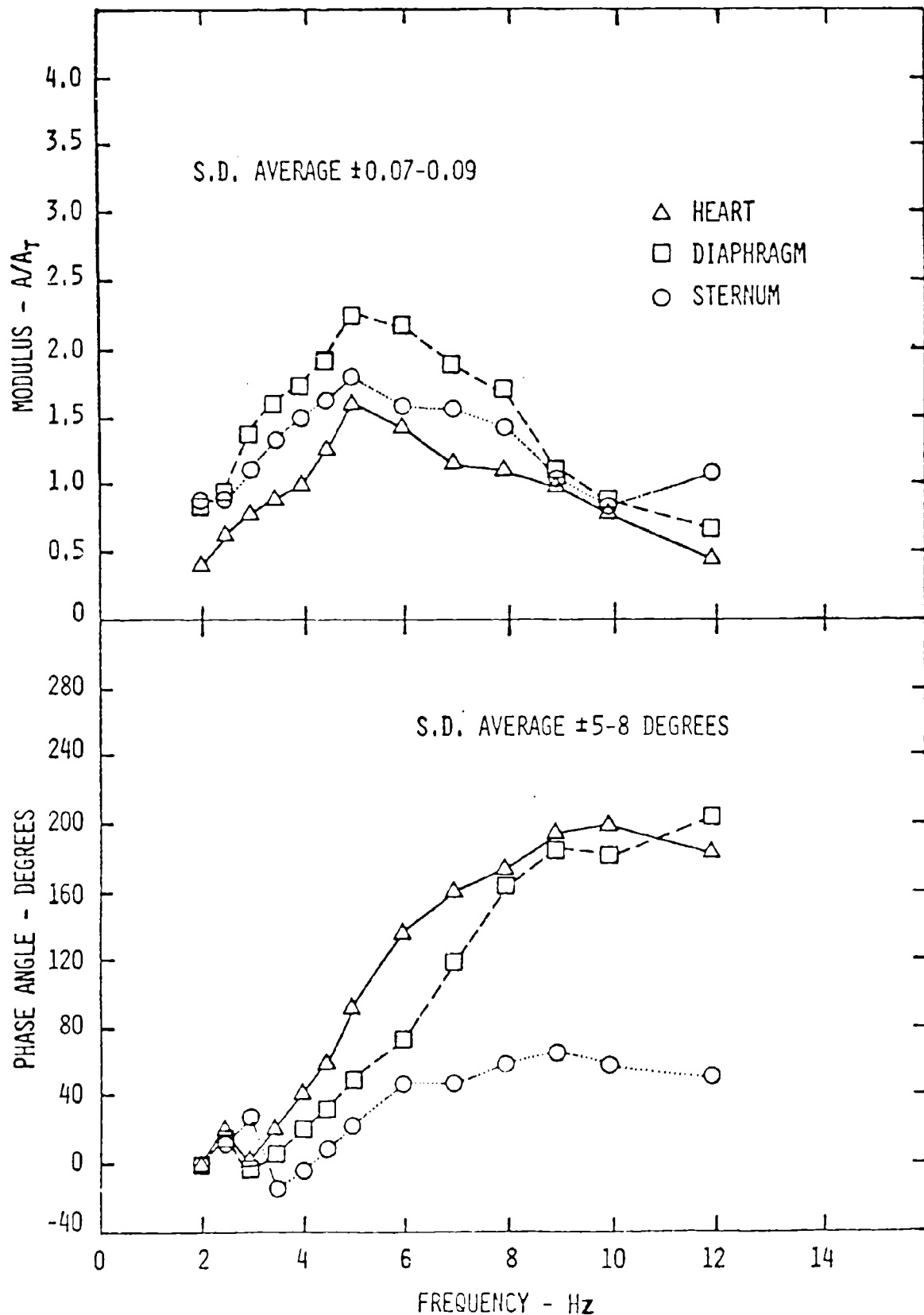ACCELERATION TRANSMISSIBILITY, 0.75 to 1.25 G VERTICAL



Fig. 1. Acceleration transmissibility modulus and phase angle of the heart, diaphragm, and sternum versus vibration frequency (animal restrained vertically).
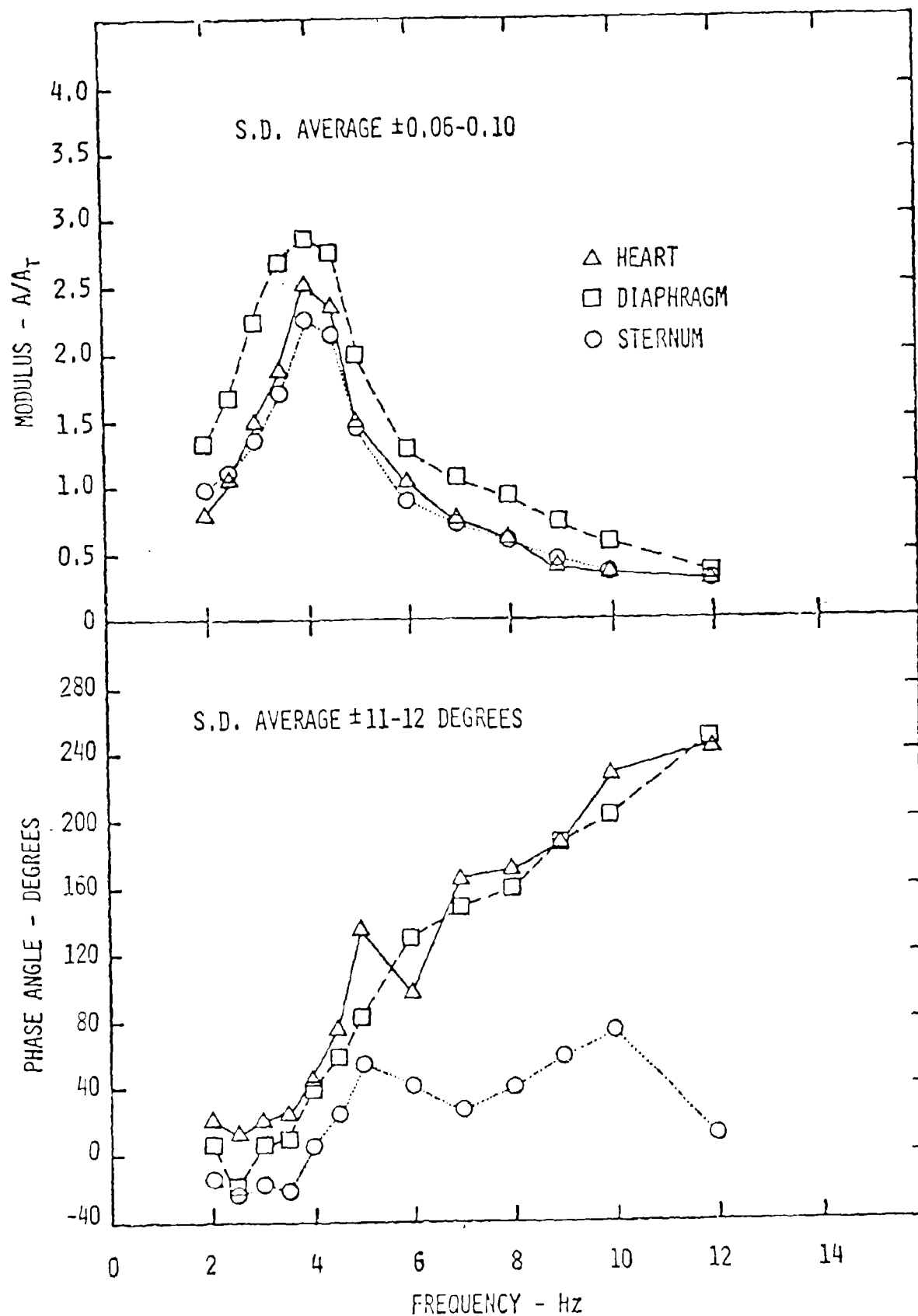
Fig. 2.  Acceleration transmissibility modulus and phase angle of the heart, diaphragm, and sternum versus vibration frequency (animal restrained horizontally).

The S.D. values generally fell within the limits of the symbols used to represent the data point. In Figure 3, the diaphragm response from Figure 1 and 2 is re-plotted for a comparison of vertical and horizontal TM and TPA.

The TM curves for all three anatomical sites exhibited a characteristic shape depending upon which vibration mode, horizontal or vertical was employed. The horizontal TM showed a rapid increase with frequency to a distinct "resonant" peak, followed by a graded decrease at high frequencies, while the vertical response showed a slower increase to a less-distinct peak, followed by a gradual decrease at higher frequencies. The vertical response seemed to be more evenly distributed over the frequency range from 2 to 10 Hz. In general, it was found that the TM of the diaphragm, heart and sternum tended to be higher for the horizontal case than for the vertical case: as much as 90% higher for the peak response of the heart and diaphragm. The primary resonant frequency for the three anatomical sites was higher for the vertical vibration mode, occurring at a frequency of 4-6 Hz compared to the 3-4 Hz for the horizontal case. The response of all three anatomical sites beyond 10 Hz was esentially damped. Beyond 12 Hz the responses of the accelerometers placed on the heart and diaphragm were due to the heart's beating action rather than the table motion. TPA was similar for both the horizontal and vertical vibration mode. Heart and diaphragm appeared to "track" together through the entire frequency range. At all three anatomical sites, PA increased from zero at low frequencies near 2 Hz (inert mass response) through 90° near the resonant frequency.

For those preparations in which intravascular aortic, intrathoracic, and transmural pressures were measured, perturbations that were evident in aortic pressure appeared to be a direct result of diaphragm "pumping" caused by the vibration input. Intrathoracic pressure fluctuations correlated directly with diaphragm acceleration (an index of diaphragm motion), tending to be greater
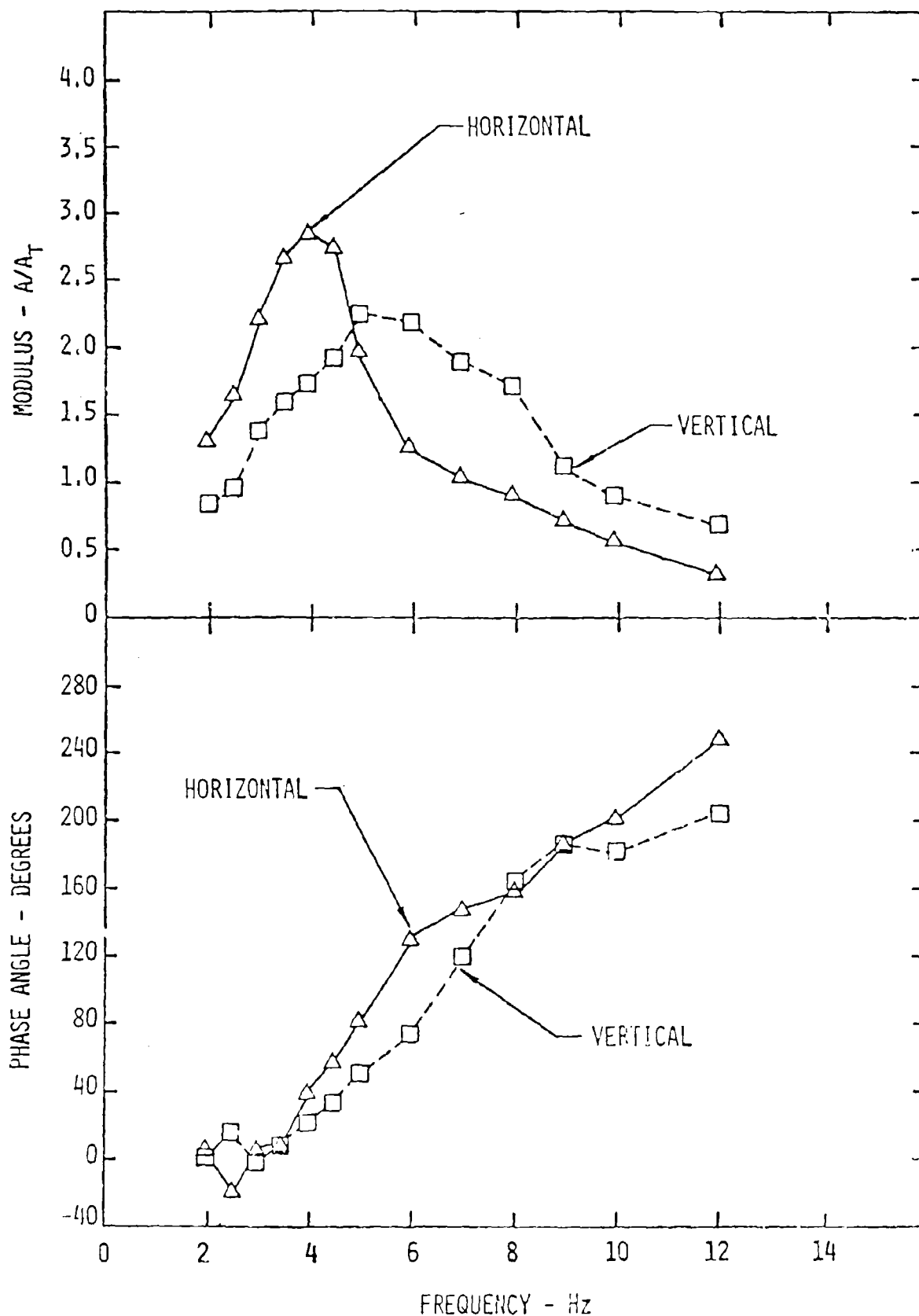
DIAPHRAGM TRANSMISSIBILITY, 0.75 to 1.25 G



Fig. 3. Acceleration transmissibility modulus and phase angle of the diaphragm (animal restrained horizontally and vertically).
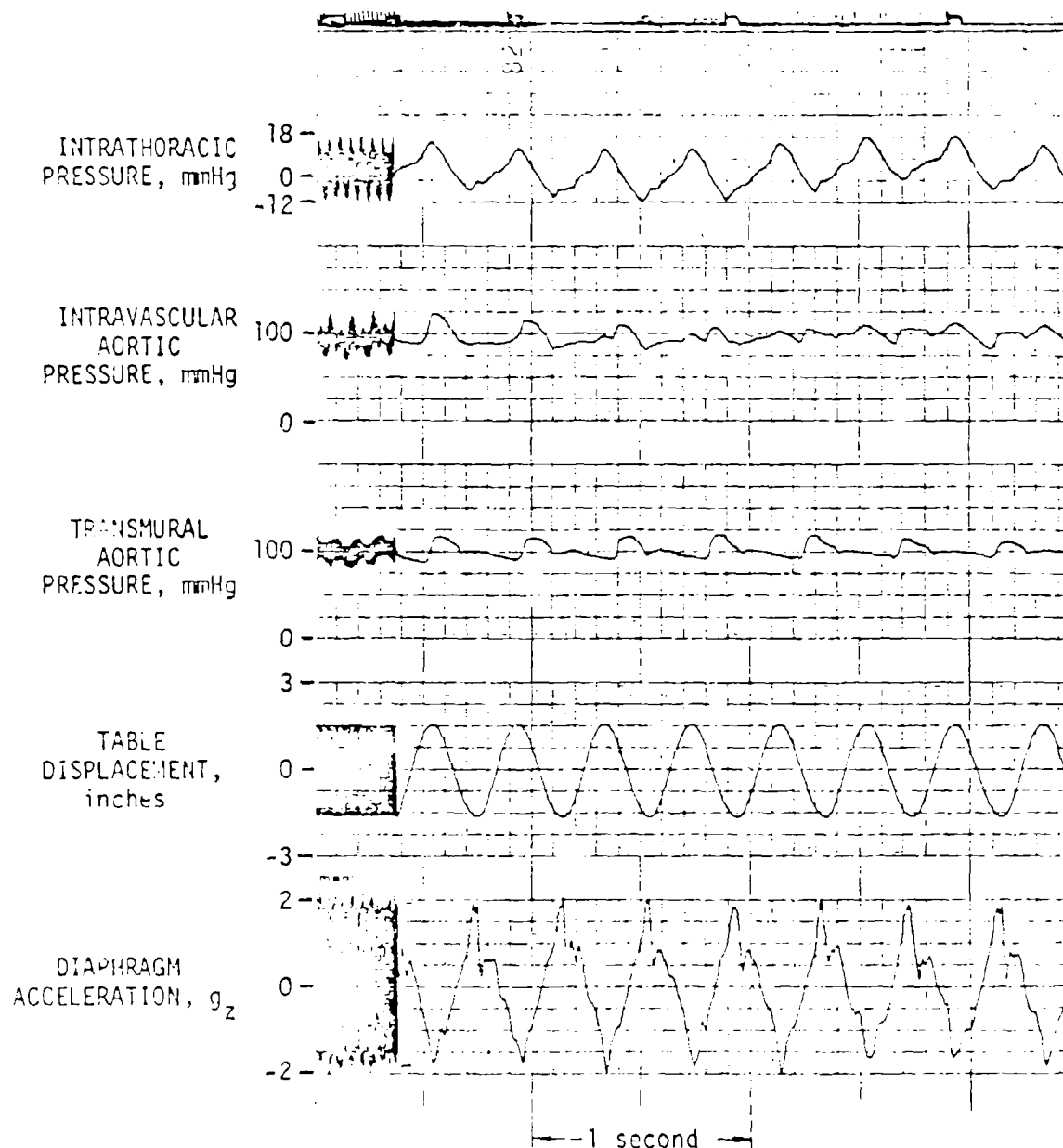
INTRATHORACIC PRESSURE, mmHg — 18, 0, -12

INTRAVASCULAR AORTIC PRESSURE, mmHg — 100, 0

TRANSMURAL AORTIC PRESSURE, mmHg — 100, 0

TABLE DISPLACEMENT, inches — 3, 0, -3

DIAPHRAGM ACCELERATION, $g_z$ — 2, 0, -2

— 1 second —

Fig. 4. Example of vibration-induced intrathoracic pressure oscillations:

1.0 $g_z$, 2.5 Hz horizontal mode, control aortic b.p. 118/92 mm Hg.

in amplitude for greater diaphragm accelerations.  Transmural pressure, the difference between intravascular aortic and intrathoracic pressure had the "normal" wave shape for an aortic pulse train (ref. Figure 4).

## DISCUSSION AND CONCLUSIONS

The following observations may be made from the results of these transmissibility studies.

1) Posture has a significant effect upon the transmission of sinusoidally applied whole body vibration to body subsystems. The TM-frequency response curves have a characteristic shape depending upon which vibration mode, horizontal or vertical, is employed.  With horizontal vibration the thoracic and abdominal masses are freer to "sloush about" (less effective) internal constraint) so that the TM (gain) near body resonance 3-4 Hz is high; while internal damping of higher frequencies, above 8 Hz is more effective than for vertical vibration. In the vertical vibration mode the $+1$ $g_z$ bias due to gravitational force seemingly acts as a restraint to motion of the thoraco-abdominal mass, for input acceleration levels of 0.75-1.25 g, so that the TM response is more evenly spread out over the input frequency spectrum with a lower peak TM at a higher resonant frequency, 4-6 Hz.

2) There is a significant amplification of input acceleration near resonance, (TM may range from 2.0 to 4.0 for a given preparation) which could have pathological consequences for situations where long term exposure or short term exposure at higher g levels is involved.

3) The thoracic and abdominal masses appear to oscillate to-
   gether as a whole, evidenced by the similarity of the TM
   and, more specifically, the TPA response curves of the heart
   and diaphragm.

4) The fluctuations in intrathoracic pressure due to the diaphragm
   "pumping" caused by vibration are of sufficient amplitude to
   suggest the possibility of vibration-induced alterations in
   the dynamics of venous return and right atrial filling.
   Further efforts will be required to evaluate this hypothesis.

E. Instrumentation and Data Acquisition Development: An Improved Technique for Determination of Left Ventricular Max dP/dt and (Max dP/dt)/P

The addition of the Raytheon 704 data acquisition and analysis system has resulted in improvements not only in the ability to accurately mean the data, but has also proved to be a more accurate technique for determining both the magnitude and time of occurrence of maximum left ventricular dP/dt. Systematic discrepancies in the magnitude of the maximum dP/dt signal occurred, whereby the computer would consistently report higher dP/dt values than those obtained through the "op-amp, Beckman Recorder" system. Suspecting the rapid sampling time (2 msec) of the computer to be reporting high frequency artifact, a small program was written to retrieve those 2 msec data points and print them out. A digitized plot (by hand) of one such pressure pulse and the corresponding difference per time ($\Delta P/\Delta t$) is shown in Figure 1. The data break in the LVP signal is a result of the computer triggering to indicate the onset of the systolic and diastolic periods of the heart signal. Several such plots were done on left ventricular pressure signals from different subjects with the following conclusions:

1) Plots of the digitized data indicated that the computer was accurately recording the LVP signal, there was no apparent artifact.

2) Plots of $\Delta P/\Delta t$ indicated that the maximum dP/dt shown by the computer was correct.

3) The maximum dP/dt occurred earlier in each heart cycle than indicated by the op-amp differentiation.

4) The roughness in the $\Delta P/\Delta t$ trace is a result of "quantization error" and could be reduced by both increasing the voltage of the signal and/or reducing the sampling rate to less than 2 milliseconds.
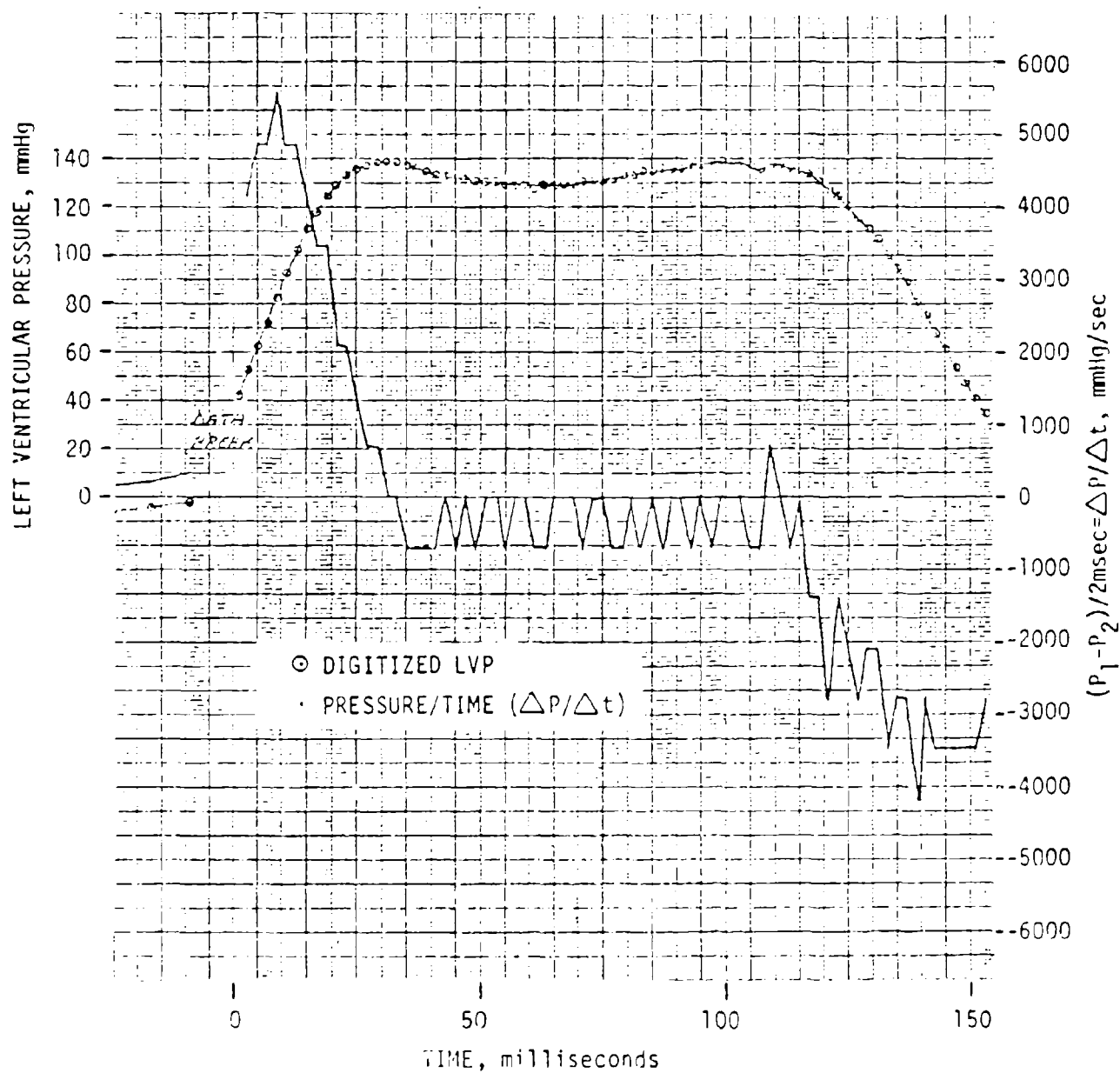
Fig. 1. Digitized plot of a typical left ventricular pressure
trace with the corresponding pressure difference/time
(ΔP/Δt).

A comparison of the analysis of a single waveform from the digitized plot, the Beckman recorder, the Honeywell visicorder and the computer dump is shown in Table I. Several of the above cited differences are apparent: the peak pressure seen in the digitized plot is the same as that of the computer dump, close to that of the Honeywell, and quite different from that of the Beckman. Maximum dP/dt as seen by the digitized plot and the computer dump agree, while that of the Beckman and the Honeywell agree, but there is a difference in the two groups of ⁻1300 mm Hg/sec. Finally, the pressure level at which maximum dP/dt occurred was considerably lower for the digitized plot than for either the Honeywell or Beckman Recorders. The ramifications of these results are obvious; the "op-amp differentiator circuit/hard-copy recorder" type system has two drawbacks, one is in the phase-lag introduced by the differentiators, and the other is in the absolute values of maximum dP/dt, seemingly a function of the inability of the pen-type recording system to accurately reproduce the sharper-sloped calibration signals.

The significance of this improved measurement technique lies not only in the increased values of maximum dP/dt, but more importantly in the accuracy of the determination of the place where maximum dP/dt occurs with respect to the left ventricular pressure trace. At least two of the indices of contractility ($\frac{\max\ dP/dt}{P}$ and $\frac{dP/dt}{@\ P_{40\ mm\ Hg}}$ ) require instantaneous knowledge of the pressure at which the derivative occurs. In some recent experiments the quantity ([maximum dP/dt]/P) has been examined and looks to be a quantity that is essentially linear, qualitatively similar in all subjects, and independent of heart rate, left ventricular, right ventricular, and aortic diastolic pressures.

## TABLE I

Comparison of Left Ventricular Variables From
A Single Beat As Determined By Several Techniques:

| Variable | Beckman Dynograph | Honeywell Visicorder | Digitized Plot | Computer Dump |
|---|---|---|---|---|
| Systolic  Period, msec | 150 | 150 | 152 | -- |
| Pressure  Peak, mm Hg | 128 | 135 | 139 | 140 |
| Maximum dP/dt, mm Hg/sec | 4194 | 4228 | 5540 | 5556 |
| Pressure @ max dP/dt, mm Hg | 113 | 106 | 79 | -- |

APPENDIX A

MODIFICATION OF CARDIAC FUNCTION BY HEART SYNCHRONOUS

WHOLE BODY VIBRATION APPLIED TO AWAKE CHRONICALLY

INSTRUMENTED CANINES

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DISSERTATION

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A dissertation submitted in partial fulfillment of the
requirements for the degree of Doctor of Philosophy
at the University of Kentucky

BY

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ACKNOWLEDGMENTS

ABSTRACT

Responses of the cardiovascular systems of awake chronically
instrumented canines exposed to whole body vibration were investigated.
Initially, studies were conducted to determine the basic nature of the
vibratory forcing function to the cardiovascular system and its time
relationship to events in the cardiac cycle. Chronically instrumented
canines were restrained with spines vertical and exposed to nonsynchro-
nous whole body vibration for a constant acceleration amplitude of 1 g
(frequency range 2-12 Hz; vibrated along $g_z$ axis; heart nonpaced). Mea-
sured and derived cardiovascular and biomechanical variables included
mean heart rate, mean aortic flow, mean aortic pressure, stroke work,
peak net force and vibration frequency. The major finding was the evi-
dence of a linear relationship between the changes in mean aortic flow
and the peak transmitted force (between the subject and the vibration
platform) divided by body weight. A linear relationship was also
indicated between changes in mean aortic flow and the log of the ratio
of mean heart rate and vibration frequency.

Experiments were then performed to determine the extent to which
synchronization of the time relationship between the input force and
the cardiac cycle, could modify cardiac function. Animals were re-
strained with spines horizontal and exposed to both nonsynchronous and
heart synchronous, sinusoidal, whole body vibration at a constant acceler-
ation amplitude of 0.75 g (ratio of vibration frequency to heart rate
was always equal to 1; vibrated along $g_z$ axis). Myocardial oxygen con-
sumption, left ventricular efficiency, time derivative of left ventricu-
lar pressure, and delay time were also included in the measured variables
in these studies. Cardiovascular responses greater or less than those
observed during nonsynchronous vibration exposures were shown to be
maintained by proper synchronization of the time relationship between
vibration and cardiac cycles, implying the capability of "dialing in"
desired responses. Significant modification of cardiac function as
reflected in parameters like cardiac work (maximum 54%) and myocardial
oxygen consumption (63%) was achieved by the application of heart syn-
chronous whole body vibration. Evidence of both hydraulic and neural

mechanisms were found to be responsible for such responses, however, the hydraulic contribution was relatively small.

In an effort to evaluate the potential of whole body vibration as a cardiac assist technique and/or exercise substitute, present data were compared to those of other assist techniques and exercise. Similarities between vibration-induced cardiovascular responses and those occurring with exercise were observed. Myocardial oxygen consumption was increased by an average of 42% for the nonsynchronous exposures and increased to a maximum of 63% for the synchronous case- a phenomenon generally seen during exercise. It is suggested that whole body vibration may have potential as a technique to prevent the cardiovascular deconditioning resulting from bedrest or weightlessness encountered during space flight. When a comparison of data from this study was made with other noninvasive and invasive assist techniques, the range of changes of various cardiovascular variables was greater. This implies that heart synchronous vibration has more flexibility in terms of modulating cardiac responses. Clearly, future studies are warranted to establish the clinical usefulness of this assist technique.

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Author's Name

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Date

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